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## THE ORIGIN OF SYPHILIS EVIDENCE FROM DISEASED BONES

A SUPPLEMENTARY REPORT

HERBERT U. WILLIAMS, M.D.

PULFADO

During four centuries men have argued as to the place where syphilis originated. Controversy and polemic over the interpretation of old documents do not seem to have settled the question. But the study of ancient and diseased bones furnishes another method for attacking the problem, for the typical syphilitic skull gives a nearly certain means of diagnosis. Favorable specimens of long bones are also valuable, though not quite so convincing as the skull since roentgenograms of long bones with chronic osteoperiostitis and yaws are sometimes much like those of syphilitic long bones. There is a better chance for determining the antiquity of syphilis through the examination of ancient bones than is the case with any other infection. There is the further advantage that the actual lesions of the disease are preserved in museums, where they may be seen by any person interested. It is not necessary to wrestle with anachronisms and with descriptions in archaic terms, in medieval Latin or in other foreign languages.

For this reason I devoted several years to examining the evidence to be found in ancient diseased bones and the results were published in 1932.<sup>1</sup> Since then new material has come to light that makes a supplementary note seem timely. I shall not discuss here the characteristics of old dried adult syphilitic bones or the difficulties encountered in determining the antiquity of bones. Those questions were considered in the paper mentioned and I do not know of any recent important addition to the knowledge of them.

North and South America have furnished some hundreds of bones of Indians which show changes that might have been due to syphilis. Often it is not possible to be absolutely certain that the bones are syph-

---

An abstract of this paper was presented at the International Congress for the History of Medicine, Madrid, Sept. 23, 1935.

1. Williams, Herbert U. The Origin and Antiquity of Syphilis. The Evidence from Diseased Bones. *Arch. Path.* **13**: 770 (May), 631 (June), 1932.

the frontal region with erosion and new bone formation leading to formation of stellate scars. It seemed to me to be in all reasonable probability an example of syphilis nearly healed. Two tibias (with roentgenograms) from the same locality but not from the same person as the skull presented thickening due to an osteoperiostitis; these changes might have resulted from syphilis or less probably from some other agency. These specimens and other material will be the subject of a special report by Dr. Snavels and Dr. Hultom.

3. A very promising collection of specimens was submitted to me by the late Dr. Roy L. Moodie, who then was working in Los Angeles

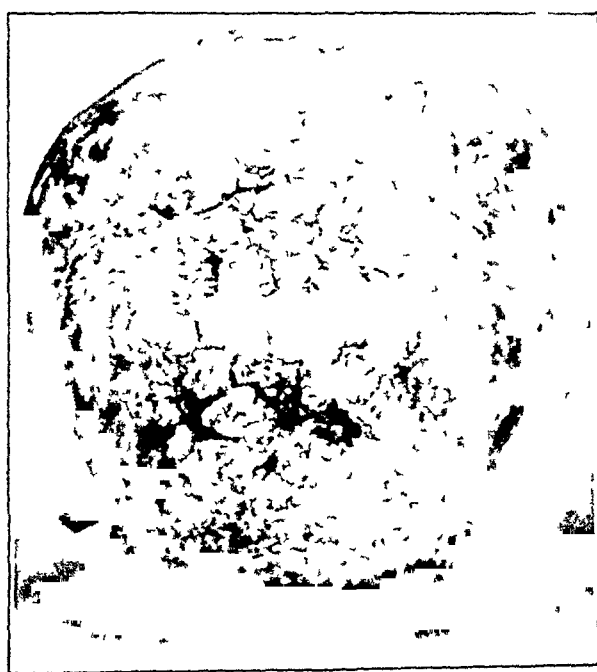
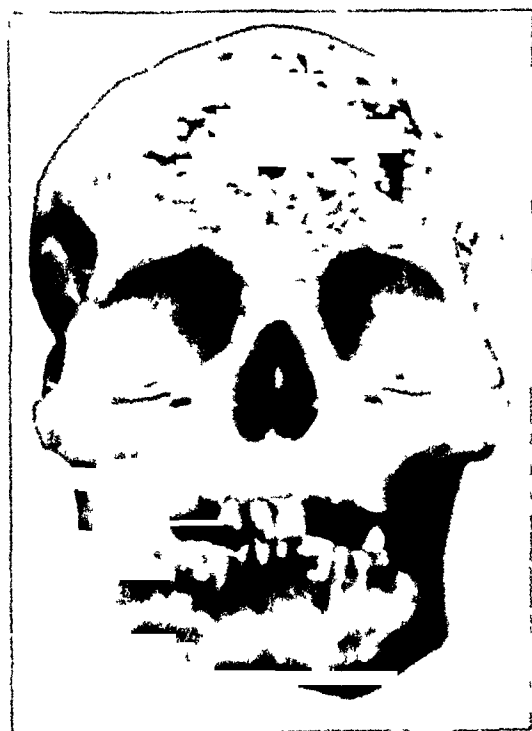


Fig. 2—A skull from Moundsville, W. Va.

under the auspices of the Wellcome Museum, London, England. The specimens were temporarily in the Los Angeles Museum, but apparently they were sent afterward to the Wellcome Museum. Dr. Moodie stated that they were part of a skeleton of a Basket-Maker Indian from Arizona and that they were probably about 1800 years old. I regret that I have no photographs and no more definite information as to their source. The specimens consisted of a skull and several long bones. At least four long bones were involved, and the changes shown in them were probably due to syphilis. The skull also probably was syphilitic, having a stellate scar that seemed quite characteristic. It was possible that the skull had also been subjected to injury, which is consistent with the

the skull, of which the more important occupies at least half of the frontal bone. The process seems to have been osseous (even for the most part), but at its edges the areas of excavation are rounded and indicate that there has been new formation of bone; it has then the characteristic worm-eaten appearance seen on some syphilitic skulls. There is a large defect in the center of the area of involvement, triangular in form, that I estimate roughly at 7.5 cm. in width and somewhat less antero-posteriorly. How much of this defect was present during life it is impossible to say—perhaps most of it (fig. 1). There was a smaller area of involvement on the left parietal bone, which did not pass through





the frontal region with erosion and new bone formation leading to formation of stellate scars. It seemed to me to be in all reasonable probability an example of syphilis nearly healed. Two tibias (with roentgenograms) from the same locality but not from the same person as the skull presented thickening due to an osteoperiostitis; these changes might have resulted from syphilis or less probably from some other agency. These specimens and other material will be the subject of a special report by Dr. Snodds and Dr. Hultom.

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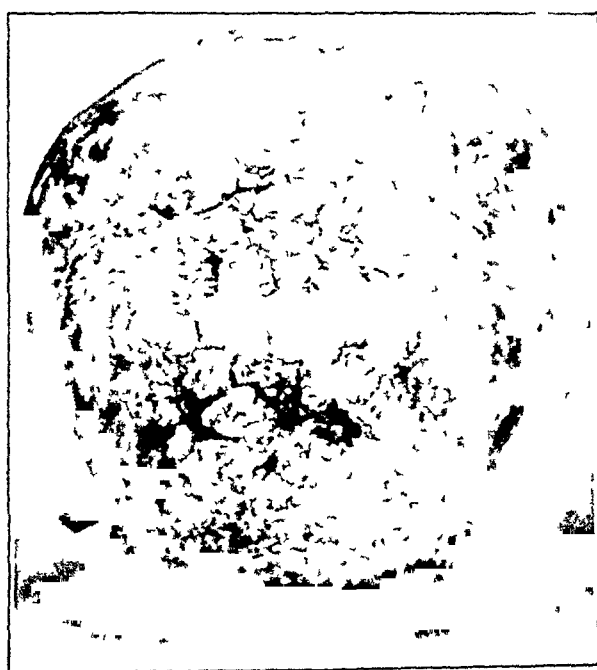


Fig. 2—A skull from Moundsville, W. Va.

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# THE VIRUS OF PEMPHIGUS AND DERMATITIS HERPETIFORMIS

ERICH URBACH

AND

STEFAN WOLFRAM

VIENNA, AUSTRIA

TRANSLATED BY FREDERICK REHM SCHMIDT, M.D., CHICAGO

This report deals with the results of investigations of material obtained from the blood serum and blisters of patients with pemphigus dermatitis herpetiformis and other dermatoses

The neurohistologic studies of Urbach<sup>1</sup> and Riehl<sup>2</sup> of tissue removed at autopsy from patients dying of pemphigus failed to demonstrate any etiologic possibilities. Kartamischew<sup>3</sup> regarded a disturbance of chloride metabolism as the cause of pemphigus, but Urbach<sup>1</sup> and others demonstrated this as untenable. Evidence in support of an endocrinologic etiology is insufficient.

An infectious cause has long been suspected. Lipschutz<sup>5</sup> found some protozoan-like formations in both blister contents and skin, but we believe that they are products of cellular degeneration, for they have been observed in bullae due to other causes.

A number of pyogenic organisms have been incriminated as etiologic agents in pemphigus. Riecke<sup>6</sup> recently reviewed the literature on this subject and concluded that none of the organisms mentioned can be proved pathogenetically responsible. Welsh<sup>7</sup> has succeeded in growing anaerobic streptococci obtained from the blood and bullae of patients with pemphigus. We are now trying to duplicate his experiments. Welsh also produced bullous eruptions in animals with this material. Our experience has demonstrated, however, that anaerobes do not occur in blood serum and blister fluid although we admit that we did not use Welsh's medium of brain tissue.

---

1 Urbach, E., and Uiberall, H. *Dermat Wchnschr* **89** 1227 (Aug 14) 1929

2 Riehl, G., Jr. *Dermat Wchnschr* **89** 1327 (Sept 14) 1929

3 Kartamischew, A. *Arch f Dermat u Syph* **143** 184, 1923, **146** 229, 1924, **148** 69, 1925

4 Urbach, E. *Arch f Dermat u Syph* **150** 52 1926

5 Lipschutz, B. *Arch f Dermat u Syph* **153** 350, 1927

6 Riecke, E. *Handbook of Skin and Venereal Diseases* Berlin, Julius Springer, 1931, vol 7

7 Welsh, A. L. *Proc Staff Meet, Mayo Clin* **9** 369 (June 20) 1934

Lanford<sup>8</sup> believes that the cause of pemphigus is an invisible virus similar to that of herpes. Definite proof that pemphigus and dermatitis herpetiformis of Duhring are both due to a filtrable virus was first brought forward by Urbach and Reiss<sup>9</sup> and later developed by Wolfiam<sup>10</sup>. Successful transmission to animals by Kumer<sup>11</sup> and Castoldi<sup>12</sup> corroborates these findings.

#### TECHNIC OF ANIMAL EXPERIMENTS

Whenever possible we used material obtained from the contents of spontaneous blebs. In lieu of this, blood serum was used. In the absence of fresh blisters a 70 per cent potassium iodide ointment or a cantharides plaster was applied to pigmented areas of skin which had previously been affected, but blisters frequently failed to appear with this method. It is inadvisable to give iodine internally, for a serious exacerbation may ensue.

Patients who have received more than just a minimal quantity of arsenic should not be used for investigation.

It is best to obtain material from fresh blisters before the patient shows elevation of temperature. The blister is cleansed with ether, alcohol and a strong solution of iodine, and the fluid is drawn into a sterile syringe with a fairly thick needle. This fluid should be injected immediately, as clots of fibrin soon form to vitiate results.

The blood serum, withdrawn as aseptically as possible, is separated by centrifugation in sterile tubes and injected into the animal at once.

All material for inoculation must be tested for sterility not only by direct smear and dark-field observation but also by implantation on various culture mediums under aerobic and anaerobic conditions. In our study only material which was sterile after ten days' incubation was used.

A 10 per cent suspension of brain tissue in a physiologic solution of sodium chloride is used to secure passage through animals. The brain is removed from a sick animal under strict asepsis, and 1 part of this is ground up with 10 parts of the sodium chloride solution, the resulting emulsion being then tested for sterility.

From a practical standpoint the test for sterility is not necessary. If the smear is free from organisms the animal should be given the injection immediately, since contamination of this material was found in only 3 of 400 cases.

Material secured at autopsy for inoculation into animals must be filtered through filter candles having an average bore of 0.08 micron. Filtration is accomplished by using a water pump with the stream under a pressure of 50 mm of mercury. One per cent suspensions of brain tissue should be employed, for the candles will not readily pass higher concentrations. This also pertains to the contents of long-standing blisters which contain a good deal of fibrin. Only

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8 Lanford J. *South M J* **21** 35 (Jan) 1928.

9 Urbach E. and Reiss F. *Arch f Dermat u Syph* **162** 713 1931.

10 Urbach E. and Wolfram S. *Med Klin* **29** 1619 (Nov 24) 1933, *Acta dermat-venereol* **15** 120 (April) 1934. *Arch f Dermat u Syph* **170** 389, 1934. *Klin Wchnschr* **13** 1265 (Sept 8) 1934.

11 Kumer L. *Skin and Venereal Diseases* Vienna, Urban & Schwarzenberg, 1933 vol 3.

12 Castoldi F. *Gior ital di dermat e sif* **73** 237 1932.

fresh blebs give good results. The material should be tested for sterility both before and after filtration. Fluid from contaminated blisters may therefore be used.

Material was sent to Herzberg,<sup>13</sup> but he was unable to demonstrate the suspected virus by staining with Victoria blue.

The subdural route should be employed for inoculation since intravenous injections gave us indifferent results. Bernhard<sup>14</sup> chose the intravenous route in his studies and obtained uniformly negative results. With the animal under ether anesthesia a needle is introduced into the subdural space in the suboccipital region, and 10 or 12 drops of spinal fluid are allowed to flow off. The test material is then injected slowly. We found that 0.5 cc is the optimal quantity, although a little experience enables one to introduce 1 cc safely. Only 12 of 400 rabbits succumbed to intracranial hemorrhage, which makes the use of the suboccipital route relatively safe.

Male rabbits weighing from 1,500 to 2,000 Gm were used in these experiments.

#### RESULTS OF ANIMAL EXPERIMENTS

*Transmission from Human Beings to Animals*—It should be understood at the outset that it is impossible to transfer pemphigus in the form in which it appears in human beings to animals, for bullae cannot be reproduced in them.

TABLE 1—Results of Inoculations of Material from Patients with Pemphigus, Patients with Dermatitis Herpetiformis and Patients with Other Diseases of the Skin into Animals

Disease	Total No of Cases	Cases in Which Inoculations Gave Positive Results	Cases in Which Inoculations Gave Negative Results	Percentage of Positive Results
Localized pemphigus	2	2		100
Pemphigus vulgaris	12	11	1	91.8
Dermatitis herpetiformis	20	14	6	70
Bullous toxic eruption				
Hysterical pemphigus				
Arsenical pemphigus				
Vesiculopapular urticaria				
Lichen ruber planus pemphigoides	10		10	0
Chronic pyoderma simulating pemphigus				
Bullous chicken tuberculosis				
Bullous grass dermatitis				
Other dermatoses	8		8	0

Animal pemphigus is characterized by a clinical and anatomic picture well recognized as that of pemphigus by workers in this field.

The total number of animal experiments performed since 1930 is 34 (table 1). Fourteen of these were made with material from cases of pemphigus and 20 with material from cases of dermatitis herpetiformis. Positive results were obtained in 91.8 per cent of cases of pemphigus and in 70 per cent of those of dermatitis herpetiformis. An inoculation was considered to have given a positive result whenever

<sup>13</sup> Herzberg K. Zentralbl f Bakt (Abt 1) **131** 358 (Mar 7) 1934.  
<sup>14</sup> Bernhard R. Acta dermat-venereol **14** 165, 1933.

the rabbits exhibited flaccid or spastic paralysis of the extremities appearing at least two days after the injection. The latter condition is imposed in order to exclude the possibility of an animal becoming paralyzed through trauma at the time of the subdural injection.

The subdural introduction of blood serum and fluid from spontaneous as well as from artificial blisters gave negative results in 10 cases of bullous dermatoses and 8 cases of other diseases of the skin.

A transmission may therefore be regarded as positively indicative of pemphigus or dermatitis herpetiformis, but a negative result, since such a result occurs in approximately 25 per cent of cases of pemphigus, should not mitigate against a clinical diagnosis of typical pemphigus. There are many reasons for negative results. In the absence of insufficient blister fluid, blood serum has to be used, so that caution should be exercised in interpreting a negative outcome. The possibility of a technical failure in not injecting the material subdurally must also be considered. It is difficult to explain a negative result when all the conditions have been properly fulfilled. As we stated in an earlier article, the formation of blebs may be the organism's attempt to rid itself of an infectious agent, in the sense implied by Aschoff. This hypothesis may also explain the varying amounts of virus found in bullae at different times. Another source of failure lies in the use of old, long-standing bullae in which autofermentative processes have weakened or destroyed the virus. In using blood serum it should be remembered that the blood probably carries only minimal amounts of virus and that these quantities vary from time to time, whereas an ectodermatropic virus will naturally concentrate in the bulla. As was stated, previous treatment with arsenic is a contraindication for these experiments, nevertheless, some patients persist in lying about this matter. Some strains of rabbits are apparently immune to pemphigus virus, as in the case of herpes. From these considerations it is evident that a negative result in a case in which pemphigus is suspected should induce one to repeat the experiment under more favorable conditions.

Table 2 shows that in 92 per cent of rabbits inoculated subdurally with unfiltered fluid from blisters either flaccid or spastic paraplegias developed, while in 82 per cent the disease progressed fatally, the cause of death being encephalomyelomeningitis. These percentages were reduced to as low as 50 per cent when filtered fluid was used. This low incidence was due to unavoidable physical factors occasioned by filtration. Inoculation with blood serum gave even poorer results as evidenced by a comparison of unfiltered serum (64 per cent paraplegias and 41 per cent deaths) with filtered serum (60 per cent pareses without deaths).

The best results in transmitting the infection from the human being to animals (first passage) are obtained by subdural introduction of unfiltered fluid from a bulla

*Second Passage (Transfer from Animal to Animal)*—Attempts were made to transfer the suspected virus from one animal to another. The results are shown in table 3. Eighty-five per cent of 26 rabbits inoculated subdurally with unfiltered suspensions of brain tissue exhibited spastic pareses, and 61 per cent died. Unfiltered suspensions had not been forced through a porcelain candle. The corresponding figures for animals given injections of filtered brain tissue are 55 per cent and

TABLE 2—*Results of Experiments with Blood Serum and Fluid from Blisters (First Passage)*

Material Used for Subdural Inoculation	Total Number of Animals	Number That Remained Healthy	Number Sick But Not Paralysed	Number Paralysed	Number Recovered	Number That Died
Unfiltered fluid from blisters	51	4	0	47	5	42
Unfiltered blood serum	22	6	2	14	5	9
Filtered fluid from blisters	10	1	1 (died later)	8	4	5
Filtered blood serum	5	2		3	3	

TABLE 3—*Results of Experiments with Brain Suspensions (Second Passage)*

Material Used for Inoculation (Passage II)	Total Number of Rabbits	Number That Remained Healthy	Number Sick But Not Paralysed	Number Paralysed	Number Recovered	Number That Died
Unfiltered brain suspension (subdural)	26	4		22	6	16
Unfiltered brain suspension (intravenous)	3	1		2		2
Filtered brain (subdural)	14	6		8	2	6
Filtered brain (intravenous)	6	2		2	2	1

43 per cent. Sixty-seven per cent of animals given intravenous injections of unfiltered material exhibited nervous symptoms. All of these perished. Filtered material produced a disease of the central nervous system in only 50 per cent of the animals. Of these 17 per cent succumbed to the infection.

*Third Passage (Transmission from Animal to Animal)*—Of 9 rabbits used for the third passage 6 became paretic of which 3 recovered and 3 died. Two of these perished in extreme cachexia, while the third succumbed to progressive paralysis. In the German manuscript a paradigm of a typical passage is presented showing the transfer of the infection from a patient with dermatitis herpetiformis to a rabbit and its further passage through animals.

## SYMPTOMS OF EXPERIMENTAL PEMPHIGUS IN ANIMALS

It appears from the observation of 258 animals inoculated with material from patients with pemphigus and dermatitis herpetiformis and in addition 30 animals given injections of fluid from other dermatoses for purposes of control that the disease manifested by rabbits takes one of two forms. The majority of animals in the first passage as well as of those receiving human virus became sick within three to seven days and either the flaccid or the spastic type of paralysis developed. A much smaller number perished in extreme cachexia.

The initial sign of disease is that of limitation of motion. Because of lack of space it is impossible to describe these movements, but we are indebted to Dr. Preissecker for a motion picture of these animals. A rabbit normally moves by a combination of hops and jumps, but the sick animal cannot jump and pulls himself along by advancing one hind leg ahead of the other. The front legs are not affected at first, but after a few days they also become paraplegic.

The next phase is dominated by a spastic paraplegia of the hind-legs. The animals jump around normally, but they can hop only a little distance, for their hindlegs are maximally contracted, rigid and resistant to passive movements. Their movements are further characterized by a marked lifting of the hindermost leg, making them limp in a peculiar fashion.

This is succeeded by a flaccid type of paraplegia of the hindlegs, which is soon followed by paraplegia of the front extremities. The front legs pull the whole body forward, finally this stops, and the animal cannot move. If the animal is not killed at this point, the respiratory center is soon paralyzed.

Severe spasms characterized by opisthotonos occasionally dominate the picture just before death. They were noted especially in those animals in which the period of incubation was short—three or four days. They were not observed in rabbits showing a protracted course of the illness, in which parietic manifestations were late in appearing.

The other form of the disease exhibited by rabbits inoculated with pemphigus material is characterized by cachexia which sets in usually during the third week of sickness. This terminates fatally in two or three weeks. The average loss of weight displayed by animals afflicted in this manner is about 500 Gm daily. The asthenic condition grows progressively worse so that finally the animals are too weak to move and they consequently appear to be paralyzed. This cachectic form seldom occurs in animals inoculated with human virus but rather frequently in passage animals.



## PATHOLOGIC ANATOMY AND HISTOLOGY OF ANIMALS EXPERIMENTALLY INFECTED WITH PEMPHIGUS

*Central Nervous System*—The following macroscopic and histologic alterations were observed in animals inoculated with material from patients with pemphigus and dermatitis herpetiformis irrespective of whether they became paralyzed or cachectic. The observations were identical in all passage animals regardless of whether they had been infected with filtered or unfiltered material.

*Gross Pathology* The membranes as well as the brain and spinal cord showed signs of severe involvement. The dura mater was congested and swollen while the pia appeared lusterless. The vessels everywhere were distended with blood. In some cases large gray clumps of exudation were seen macroscopically, especially at the base of the brain. Similar alterations occurred in the membranes of the spinal cord, though to a lesser degree. On section the brain was edematous, and many ecchymoses stood out on the cut surface. These could be removed with a knife. Marked hyperemia of the gray matter was present throughout the length of the cord, bringing the white matter into relief.

*Histology* The histologic picture was that of a disseminated, non-purulent encephalomyelomeningitis. The pia mater was swollen, and its vessels, especially the veins, were maximally distended. Figure 1 *A* illustrates the perivascular accumulations of cellular infiltration between the pia and the arachnoid. These cells were chiefly large mononuclear, lymphocytic and plasma cells. Pus cells were seldom seen and then only in animals which had been sick only a few days. The absolute quantity and character of the infiltration varied greatly. A slight sero-fibrinous exudate might be scarcely visible on the surface, although at the base of the brain it was usually more marked. The accumulation of pus cells and fibrin was greatest along the large vessels, and in tracing the course of such a vessel it was seen that the perivascular infiltrate persisted far into the brain.

The brain was hyperemic and swollen, as evidenced by the maximally dilated blood vessels. Some sections showed extravasations of blood into the parenchyma, which explains the ecchymoses seen on gross section (fig 1 *B*). The perivascular infiltrations composed chiefly of lymphocytes were the most prominent alterations. The vessels (fig 2 *A*) were surrounded by a cloak of these cells (fig 2 *B*). Few leukocytes were seen. Thromboses were found occasionally. Independent foci of inflammation were seen at some distance from the vessels, which showed proliferation of connective tissue cells in addition to the cells mentioned (fig 3). In serial sections however this apparent independence fell away for the connection of these foci with vessels became



Fig 1—*A* dermatitis herpetiformis (rabbit 103) Meningitis at the base of the pons in a passage animal inoculated subdurally with a filtrate of brain suspension. Low power magnification. *B* pemphigus (rabbit 24) Cortical hemorrhage in a passage animal inoculated subdurally with blister fluid. Low power magnification.



Fig 2—*A*, dermatitis herpetiformis (rabbit 35) Marked perivascular infiltrations in the region of the hippocampus in a passage animal inoculated subcutaneously with filtered blister serum. Low power magnification. *B*, dermatitis herpetiformis (rabbit 35) Marked perivascular infiltrations around a cerebral vessel in a passage animal inoculated with filtered blister fluid. High power magnification.

evident. These perivascular accumulations tended to form nodules on the undersurface of the ventricles, especially in the presence of small vessels with thrombosis (fig. 4). Such areas of encephalitis were present in all cases, although not so numerous as in the brains of rabbits inoculated with the virus of herpes.

The membranes of the cord were similarly affected with hyperemia and dilatation of the vessels. The exudation and fibinous accumulation on the pia were slight. The marrow appeared swollen on section, while the gray matter showed hyperemia and ecchymoses. Figure 5

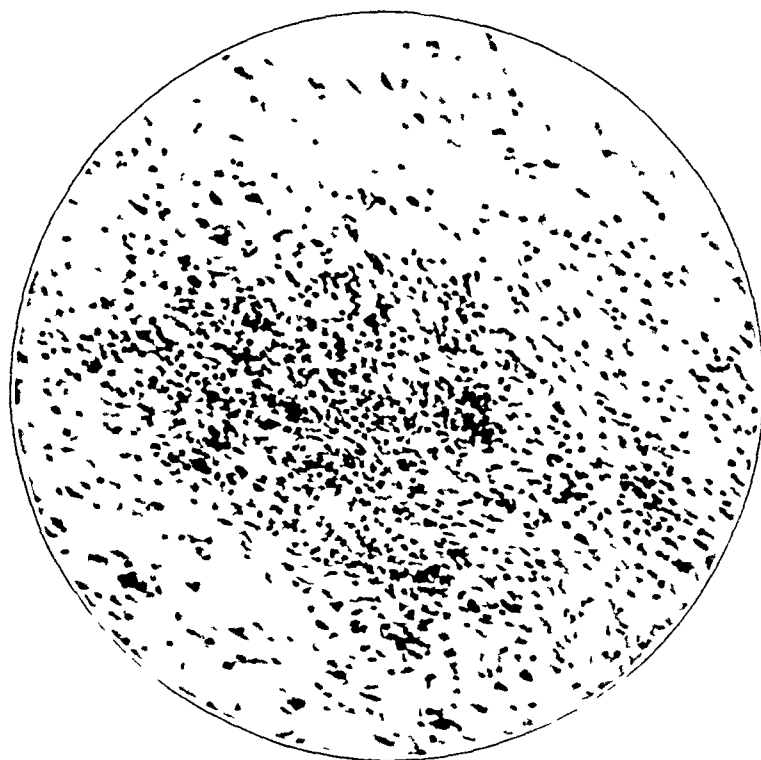


Fig. 3—Dermatitis herpetiformis (rabbit 35). First passage. Subdural inoculation with filtered blister fluid. Large area of encephalitis in the parietal lobe. High power magnification.

illustrates the slight degree of perivascular infiltration which was similar in structure to that seen in the brain.

We were unable to demonstrate inclusion bodies in any of this material although the most modern staining methods were employed.

*Other Organs*—Histologic examinations were made of the spleen, liver, lung, heart and kidneys. While the alterations in the central nervous system were definitely of an inflammatory nature, those in other organs of the body, with the exception of the lungs, were frankly toxic in character.

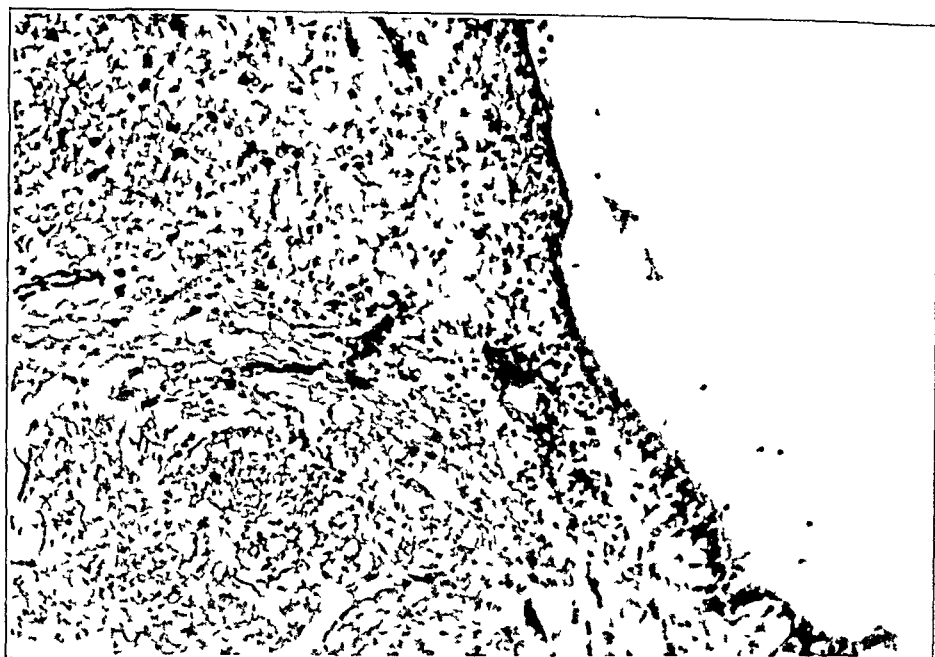


Fig 4—*Pemphigus vulgaris* (rabbit 160) Second passage Subdural inoculation with filtered brain suspension Subependymal lesion High power magnification

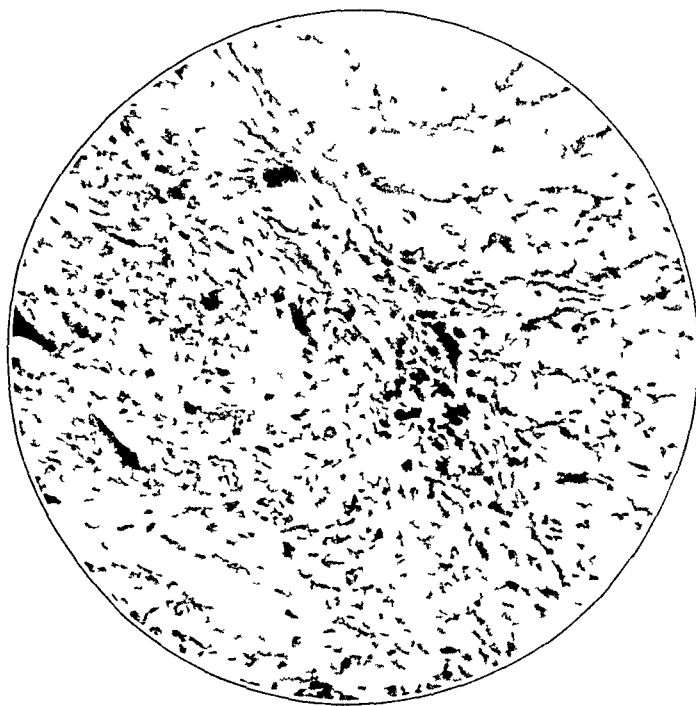


Fig 5—*Pemphigus vulgaris* (rabbit 840) First passage Intravenous inoculation with blister fluid Lesion of myelitis in the anterior horn of the thoracic region High power magnification

All animals perishing with paretic symptoms showed evidences of pulmonary edema. The distended alveoli with intact epithelium contained a foamy albuminous fluid, staining deep red with eosin. Only an occasional leukocyte was seen. The picture was that of an agonal edema.

#### THE PRESENCE OF VIRUS IN AUTOPSY MATERIAL

The virus was demonstrated in two patients with pemphigus, and when they died various organs including healthy and diseased skin were used in testing for the presence of virus.

Blood removed from the heart after death and pieces of skin, mucous membrane, spleen and lymph nodes were investigated. This material was obtained three hours after death. The serum was separated by centrifugation and filtered through Berkefeld candles. The skin and other organs were stripped of fat, cut into small pieces and ground with quartz sand into an emulsion with physiologic solution of sodium chloride in the ratio of 1:20, after which it was forced through candles. Tests for sterility were made as previously described.

The animals were inoculated subcutaneously under ether anesthesia with 0.5 cc of this material. Two animals were given the filtrate of each organ.

*Transmission of Human Virus Obtained at Autopsy to Animals (First Passage)*—1 Both rabbits inoculated with filtered serum obtained from the first patient (hereafter referred to as patient 1) died within twenty hours without showing clinical symptoms. One animal inoculated with serum from the second patient exhibited a paraplegia of its hindlegs but recovered after two days. The other animal remained well.

2 One rabbit given an injection of a filtrate of diseased skin from patient 1 died of complete paralysis after forty-eight hours while the other remained healthy. Both animals receiving material from patient 2 died after twenty-four hours completely paralyzed.

3 All animals inoculated with filtrates from normal-appearing skin remained well.

4 Filtrates of lymph nodes from both patients produced severe paralysis from which one animal recovered.

5 The filtrate of mucous membranes of patient 1 produced typical paresis with death on the sixth day in one animal and the second animal appeared normal. Both rabbits given the filtrate of mucous membranes of the second patient perished in twenty-four hours.

6 Splenic filtrates caused paresis in both animals: the one dying in six days and the other in twenty-four hours.

For purposes of control we inoculated rabbits with filtered material obtained at autopsy from other patients of equivalent ages. Of these patients, 4 had died of cerebral hemorrhage, 2 of tumor of the brain and 1 of carcinoma of the ovary. Sixteen animals were used, all of which remained healthy.

*Passage Through Animals (Second and Third Passages)*—The second passage was successful with filtered serum (patient 1), diseased skin (patients 1 and 2), diseased mucous membrane (patient 2), filtrate of lymph node (patients 1 and 2) and splenic filtrate (patients 1 and 2).

The third passage was successful with diseased skin (patient 2) and splenic filtrate (patients 1 and 2).

*Pathologic Anatomy*—The animals that perished in these studies exhibited pathologic anatomic alterations similar to those inoculated with material obtained from living patients. The changes were those of a meningo-encephalomyelitis (fig 6). They were of greater severity than the alterations found in the brains of animals inoculated with filtrates of living tissues. This may have been due to the action of necrotoxins superimposed on that of the virus, thus accounting for the early onset of symptoms and death in some animals.

In summarizing it may be stated that rabbits inoculated with filtrates of diseased skin, mucous membrane, lymph nodes and spleen exhibited symptoms similar to those shown by rabbits given injections of fluid from blisters of patients with pemphigus and dermatitis herpetiformis. A second passage was successful in many animals, a third, in only a few. The histologic observations were those of meningo-encephalomyelitis. All control experiments yielded negative results, including that made with a filtrate of skin uninvolved by the disease process. It should be emphasized that a number of animals displaying clinical symptoms failed to reveal any pathologic alterations of the central nervous system.

#### SEROLOGIC DEMONSTRATION OF ANTIBODIES IN THE VIRUS

We collaborated with R. Brandt of the serodiagnostic laboratory in performing the following investigations:

The methods employed in demonstrating the presence of a virus in diseases such as herpes served to guide us in studies carried out on the pemphigus group. Two avenues of approach to this problem are available. 1. Blood serum may be tested for antibodies by mixing it with tissue containing antigen. 2. The fluid from blisters and the extracts of various organs of human beings and animals may be tested for antigen by mixing with serum known to contain antibodies.

The second method presupposes the presence of antibodies in the blood serum of patients with pemphigus and dermatitis herpetiformis. Their presence is established by the complement-fixation reaction, in

which freshly inactivated fluid from a blister or an aqueous extract of brain from an infected animal is used

The test is performed by mixing the serum, which has been inactivated twenty-four hours previously, with one of the two antigens. Best results are



Fig 6—*A pemphigus vulgaris* (rabbit 230) Meningitis observed in an animal inoculated subdurally with a filtrate of lymph glands. Low power magnification. *B pemphigus vulgaris* (rabbit 231) Perivascular infiltration. Subdural inoculation with splenic filtrate. Low power magnification.

secured by using a suspension of brain tissue from rabbits showing parietic symptoms three or four days after being inoculated with the fluid from a human bulla



The animals should be killed at the crisis of the disease. It is advisable to subject the brain tissue to ether extraction for ninety-six hours before grinding it up and then let it stand for eight days at room temperature in a 0.5 per cent phenolized physiologic solution of sodium chloride in the ratio of 1:10. The test must be made quantitatively with increasing doses of antigen.

When the reaction is negative, various dilutions of blister fluid are added to blood serum known to contain antibodies, as demonstrated by the first method. The serum from fresh cases of pemphigus and dermatitis herpetiformis does not often contain antibodies at a time when the virus is demonstrable in the blisters.

In 9 cases of pemphigus, 11 of dermatitis herpetiformis and 150 of various skin and venereal diseases, including a few cases of herpes and erythema multiforme, tests were made by this procedure. Antibodies were repeatedly demonstrated in the serums of 7 patients with dermatitis herpetiformis. It required several weeks before the serum from a fresh case of pemphigus showed deviation of complement while the virus had been found much earlier in blister fluid with method 2. The reaction of the blood serum remained negative in 9 instances, while virus was demonstrated serologically in all blisters.

The circumstance that not only blister fluid from patients but also extracts of diseased skin and spleen removed at autopsy possess antigenic properties is of pathogenic significance.

All control material except that from patients with herpes and erythema multiforme gave negative results, so that it will be necessary to test these group reactions for specificity of virus.

#### IMMUNOLOGY

Investigations were carried out on 52 rabbits infected with pemphigus to ascertain (a) their immunity to pemphigus virus and (b) their immunity to herpetic virus.

TABLE 4—*Results of Tests for Immunity Following Inoculation with Pemphigus Virus*

State of Animals Inoculated with Pemphigus Virus	Total No. of Animals	Animals Subsequently Inoculated with Pemphigus Virus			Animals Subsequently Inoculated with Herpetic Virus		
		Healthy	Sick	Dead	Healthy	Sick	Dead
Remained symptom free	27	10		2	3	3	9
Slightly sick	16	2			2	1	11
Very sick	9	1		1	3		4

Many animals remained symptom-free after being inoculated with the virus (table 4). This is explained on the basis of attenuation of the infection by passage through animals, for the virus appears to lose strength in transmission. Ten of 12 rabbits of this group failed to exhibit symptoms when they were reinoculated with virus, while 2 died. These 10 animals may have possessed a natural immunity to the

virus, either congenital or acquired, although similar results obtained with herpetic virus speak for a state of silent immunization in these rabbits. A resistance to the infection was certainly present in the 25 rabbits which had shown symptoms after the first introduction of virus, for when virus was again injected only 1 of this group perished.

In testing for crossed-immunity to herpetic virus it was found that of 15 rabbits previously inoculated with pemphigus virus only 3 remained symptom-free when herpetic virus was injected while 12 exhibited nervous manifestations and 9 of these perished. The percentage of sick animals after inoculation with the herpetic virus was 80, while that with pemphigus virus was only 16.6. Similar relationships were found in animals which had recovered from pemphigus and were then inoculated with herpetic virus.

The question of crossed-immunity was studied further by introducing herpetic virus into the corneas of rabbits and, after their recovery from this sickness, infecting them with pemphigus. One animal remained symptom-free and 3 perished with parietic manifestations.

TABLE 5—Results of Tests for Crossed-Immunity to Pemphigus in Rabbits Inoculated with Herpetic Virus

Nature of Reaction to Corneal Inoculation with Herpetic Virus	Animals Subsequently Inoculated with Pemphigus		
	Healthy	Sick	Dead
Limited to cornea	1		1
Focal, with severe nervous symptoms			2

From these investigations we may conclude: 1. No crossed-immunity exists between pemphigus (also dermatitis herpetiformis) and herpes. 2. Animals recovering from pemphigus exhibit a high percentage of immunity to reinfection with pemphigus. 3. Some animals infected with pemphigus material remained clinically well, which is explained on the basis of silent immunization.

#### EXPERIMENTS WITH ACTIVE AND PASSIVE IMMUNIZATION

We are now trying to immunize patients to pemphigus and dermatitis herpetiformis in the following manner:

*Active Immunization*—A suspension of brain tissue from animals inoculated with pemphigus and showing typical symptoms of the disease is employed according to Alvisatos' <sup>1</sup> modification of Pasteur's method of vaccination against rabies.

<sup>1</sup> Alvisatos, G. P. Deutsche med. Wochenschr. 48: 295 (March 3) 1922. Zentralbl. f. Bakt. 98: 304 1926.

*Passive Immunization*—(a) Repeated transfusions are made employing the blood of a patient recovering from an attack of pemphigus or dermatitis herpetiformis (b) Repeated transfusions of immune serum from rabbits recovering from an infection are performed at short intervals

#### COMMENT

Investigations were conducted with material obtained from 34 patients with pemphigus and dermatitis herpetiformis in an attempt to prove the identity of these dermatoses with the group of diseases caused by an invisible virus. Animals inoculated subdurally with blister fluid exhibited signs of the disease in 91.8 per cent of cases of pemphigus, 100 per cent of cases of localized pemphigus and 70 per cent of cases of dermatitis herpetiformis. The histologic changes registered in the brain substance of the experimentally infected rabbits were always those of meningo-encephalomyelitis. Control experiments made with material obtained from other dermatoses gave negative results in all instances. The rabbits 288 in all were inoculated by the subdural route.

We want to emphasize the fact that animals inoculated with virus from patients with pemphigus showed the same symptoms as those into which material from patients with dermatitis herpetiformis had been introduced. Just as the course of dermatitis herpetiformis is milder in human beings, so in animals it is characterized by lesser morbidity and mortality. The symptoms exhibited by animals in conjunction with the histologic changes in the brain tissue point unreservedly to one and the same pathogenic agent as is responsible for both pemphigus and dermatitis herpetiformis. The majority of passage animals inoculated subdurally with either blister fluid from patients with pemphigus or a suspension of brain from animals infected with the disease exhibited the manifestations of pemphigus.

The symptoms and histologic changes observed in passage animals correspond exactly to those occurring in animals infected directly with human virus.

Since microscopic and cultural studies gave invariably negative results it must be assumed that we are dealing with an invisible virus necessarily filtrable because the transfer of the infection from the human being to animals and its further passage through animals was successful with filtered material.

The ectodermotropic character of the virus is demonstrated by its affinity for nerve tissue. The involvement of the central nervous system was marked in all animals infected with material obtained from patients with pemphigus in the florid stage. This circumstance accords with our findings in herpes.

The acceptance of a virus as the etiologic factor in pemphigus brings up the question of the primary tissue attacked by the virus. This tissue is probably the skin since inoculations of blister fluid were invariably the most successful. As stated, this may also be explained on the basis of Aschoff's hypothesis.

The picture composed by the symptoms and the histologic changes in the central nervous system closely resembles that produced in animals by the virus of herpes. Attempts to secure crossed-immunity between pemphigus and herpes failed, while animals which recovered from an attack of pemphigus usually displayed an immunity to reinfection with pemphigus. We also observed some animals that failed to exhibit symptoms of any kind other than resistance to reinfection with pemphigus.

The supposition that pemphigus is caused by a virus is further strengthened by the results of inoculations of animals with material obtained from the two patients at autopsy. Passage through animals was successful in both cases, the material used consisting of filtrates of normal and diseased skin, spleen and lymph nodes.

By serologic tests we were able to demonstrate that the disease manifested by our animals was the same as pemphigus in human beings. Positive complement-fixation reactions between the blood serum and brain filtrate of sick animals were obtained *in vitro* in a large majority of cases. Since this reaction also takes place when the fluid from blisters is used as antigen, the claim of an identity of the antigen in blebs and brain filtrates appears justified.

Our findings have recently been confirmed by Taniguchi, Kuga, Okamoto and Masuda.<sup>16</sup> These investigators also secured passage of the infection through animals and noted that the virulence was augmented by this procedure. Very minute round bodies similar to inclusion bodies were found in the fluid from blisters stained by Giemsa's method.

#### SUMMARY AND CONCLUSIONS

1 Rabbits inoculated with the blood serum and the fluid from blisters of patients with pemphigus vulgaris and dermatitis herpetiformis exhibited a characteristic clinical and anatomic picture. A similar disease was manifested by animals given injections of filtrates of the skin, mucous membranes, spleens and lymph nodes removed at autopsy from patients dying of pemphigus.

2 Attempts at transmission of the infection from human beings to animals and its passage through animals were repeatedly successful. The numerous successful transfers made with filtrates of fluids from

<sup>16</sup> Taniguchi, T., Kuga, S., Okamoto, S., and Masuda, Z. *Zentralbl. f. Haut- u. Geschlechtskr.* 50: 475, 1935.

blisters, blood serum and brain tissue point to an invisible, filtrable virus as the cause of these diseases

3 The blood serum of patients with pemphigus contains antibodies specific to the antigen present in the blisters of patients as well as in the brains of infected animals

4 Animal inoculations and serologic tests are therefore of diagnostic importance

5 Immunologic investigations demonstrate that a crossed-immunity between the viruses of pemphigus and herpes does not exist

6 Animals which have recovered from an infection with pemphigus are immune to reinfection. Some animals appear to have been silently immunized to the infection

7 These experiments indicate that pemphigus vulgaris and dermatitis herpetiformis are caused by one and the same virus. They represent different forms of the same disease

# AN UNUSUAL CASE OF KERATOMA SENILE

## "KERATOSIS PRAECANCEROSA"

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The first thorough investigations into the subject of keratoma senile being of comparatively recent date some addition to the knowledge of this disease is still highly desirable. Until recently only a few investigators (Dubreuilh,<sup>1</sup> Darier, Pusey and others) have distinguished between keratoma senile and verruca senilis. It was especially the investigations of Freudenthal<sup>2</sup> which rendered it possible to establish the fact that clinically and more particularly, histologically a profound difference between the classic forms of the two conditions is actually demonstrable. It was demonstrated that, in contradistinction to verruca senilis, keratoma senile is to be regarded as precanceromatous—a finding which has assigned much greater importance to this condition. It has also been shown, as a result of the systematic researches which Freudenthal's fundamental publication made possible, that keratoma senile and not verruca senilis is apt in a considerable percentage of cases "to degenerate into carcinoma a fact which gives to keratoma senile a practical importance which is not to be underrated."

For a considerable time I have been in a position to study a patient with keratoma senile and have made some observations which may make it possible to regard this condition from a new point of view.

### REPORT OF CASE

A 24 year old servant girl had suffered since her fifth year from a dermatosis on the back of the right hand. The disease had not greatly troubled her, at the most there had been a slight itching after washing the hands. However the fact that several new efflorescences had appeared on the forearm and in the bend of the elbow disquieted her and caused her to seek medical assistance. She had never been seriously ill and had never been treated with medicaments containing arsenic or with roentgen rays. There was no consanguinity between the parents or between the grandparents. Diseases of the skin had not occurred in the family.

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1 Dubreuilh. Ann. de dermat. et syph. **27** 1158 1896. Moncorps. C. Keratoma senile in Jadassohn J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer 1931 vol. 8 pt. 2 p. 425.

2 Freudenthal W. Arch. f. Dermat. u. Syph. **152** 505 1926.

3 Montgomery H. and Dorfifel J. Arch. f. Dermat. u. Syph. **166** 286 1932. (Montgomery's statistics showed that 25 per cent degenerated into carcinoma.)

with the exception that the patient's mother, who was 60 years of age, was said to have stationary scaling red patches on the backs of the hands

Examination of the patient showed that on the back of the right hand were numerous round to polygonal somewhat raised pale red lesions, some of them the size of a lentil. A number of them were covered with grayish-yellow, very adherent scales with a rough surface. The keratotic substances could with some difficulty be removed with the aid of forceps, after which slight hemorrhage occurred. It was found that the scales were regularly scratched off by the patient which accounted for the presence of the red maculae. The efflorescences were scattered over the back of the hand and fingers and were confined to several phalanges. Between the first and the second metacarpus they were densely grouped and partly run together so as to form a plaque of irregular outline and about as



Fig 1—Keratosis praecancerosa

big as a 2 shilling piece. That plaque was somewhat raised (not infiltrated), pale red (after irritation it became dark red) and, if not scratched off, covered with dry, grayish-yellow keratotic scales. The solitary efflorescences, especially on the lateral side of the thumb, displayed a tendency to spread like a ribbon, continuing with brief interruptions to the medial side of the wrist joint. From there the efflorescences continued, neatly linear, running along the median epicondyle and obliquely over the dorsal side of the forearm, half-way along which they ended. The lesions there were small and more easily felt than seen. When the gray-yellow scales were removed a sharply outlined macula, not raised above the surface of the skin, remained, which readily bled. In the bend of the elbow similar lesions formed a sharply defined median line about 2 cm in length. The efflorescences there showed a dark red edge. On the back of the hand this was less distinct and often visible only after irritation. The lesions on the forearm lacked the erythematous edge. The condition was strictly unilateral.

The normal skin was remarkably white and supple. The arms were thickly strewn with ephelides, and it is noteworthy that they were much more pronounced on the right than on the left arm. There were also on the right arm but not on the left, several flat pigmented nevi the size of a sixpence. During the observation of the patient it was on one occasion possible to see how a group of new efflorescences in the shape of small, not very clearly defined, pale red patches appeared on the first phalanx of the fourth finger. The lesion had not undergone any modifications in the last year, and no new efflorescences had made their appearance until lately.

*Histologic Examination*—A biopsy was made of one of the efflorescences on the back of the hand.

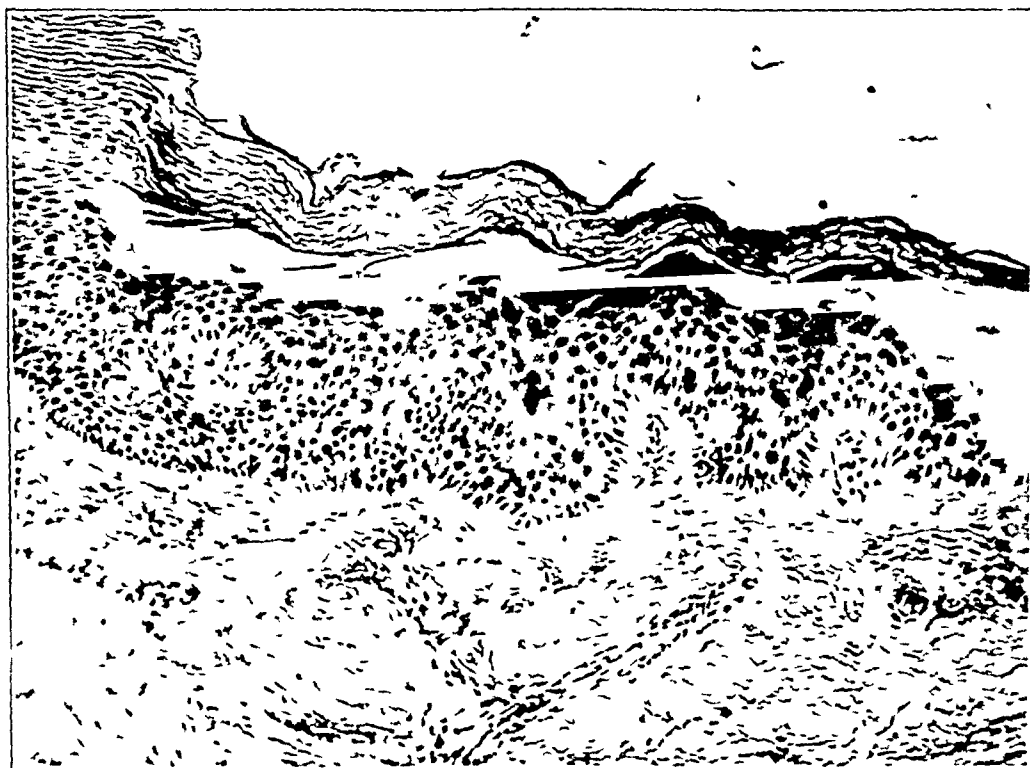


Fig 2—Microscopic appearance of a lesion from a patient with keratosis praecancerosa

**Stratum Corneum** The alternating hyperkeratotic and parakeratotic regions were sharply separated from one another. The fact that the parakeratotic scales were adherent accounted for the production in several places of fairly highly piled up layers of parakeratotic lamellae which fell off steeply on both sides, where the parakeratosis ceased, to the hyperkeratotic skin. The follicles and the ostia of the sweat glands were filled with hyperkeratotic material.

**Stratum Granulosum** The stratum granulosum was lacking where there was parakeratosis but was strongly developed in the hyperkeratotic parts.

**Rete Malpighi** Under the parakeratotic parts the rete malpighi was somewhat broadened; elsewhere it was rather narrower than normal. In the stratum basale of the attenuated parts (under the hyperkeratotic regions) were several large cells frequently with more than one nucleus. These nuclei round or oval, occasionally concave with an abundance of chromatin and containing several large



nuclear masses, were often in a vacuole and surrounded by a narrow fringe of protoplasm (clumping cells). Apart from a certain inequality in the size of the cells and nuclei, especially in the vicinity of the clumping cells, the epithelium was normal. There were few mitoses. There were no symptoms of dyskeratosis (as understood by Darier), except for a rare *corps rond*. The stratum spinosum displayed intercellular edema, which was especially prominent under the parakeratotic columns (alternating dark and light parts in the preparation).

**Cutis.** In the cutis the capillaries were enlarged, and there was slight infiltration of round cells, especially near the blood vessels. There were no signs of degeneration.

#### COMMENT

A study of the histologic picture in this case shows that it is similar to that given for keratoma senile by Freudenthal. The clinical picture of the efflorescences is also in accordance with it. The presence of the clumping cells might incline one to think for a moment of Bowen's disease. That disease may be ruled out, however, because of the almost total absence of dyskeratosis (as understood by Darier), the occurrence of clumping cells in the narrowed parts of the epidermis, the absence of the numerous mitoses and other features, while the parakeratotic columns alternating with the hyperkeratotic parts, in connection with the other pathologic changes mentioned, showed a picture similar to that of keratoma senile as described by Freudenthal.

From the point of view of the differential diagnosis arsenical and roentgen ray keratoma also must be considered. The anamnesis, however, showed no exposure to these agents, furthermore, none of the clinical characteristics peculiar to these dermatoses were present. As far as Darier's disease is concerned, both the histologic and the clinical picture showed this diagnosis to be out of the question. Such was also the case with Hopf's acrokeratosis verruciformis to which the condition bore a superficial likeness.

The only possible diagnosis was therefore keratoma senile. The remarkable point was the patient's age, especially the very early age at which the disease made its first appearance, for keratoma senile is supposed to develop on a presenile dystrophic or senile degenerated skin and to be a symptom due to the process of senescence. In this case, however, senescence was out of the question. The patient was young, the condition had first appeared at an early age and the rest of her skin was remarkably white and supple, showing no clinical trace of atrophy or other signs of senile degeneration. One therefore has the choice either of considering this to be an entirely new disease or of revising the present views on keratoma senile. The clinical and histologic features were, however, so typical of keratoma senile that one hardly seems justified in deciding that the case is an instance of a new dermatosis.

What conclusions, then, are to be drawn on the strength of the evidence here described? In the first place it is remarkable to see keratoma senile at such an early age. The question therefore arises as to whether one is justified in regarding the condition called keratoma senile simply as a symptom of senile or presenile degeneration of the skin. As a matter of fact, doubt has already been cast on this view by Dubreuilh, who showed that only three of the two hundred and fifty inmates of a home for old men were suffering from keratoma senile. On the other hand Gans,<sup>4</sup> in his work entitled "*Histologie der Hautkrankheiten*," mentioned a histologic investigation of two cases of "warts" in sisters 10 and 31 years of age, respectively. After having read Freudenthal's work, he did not hesitate to regard the symptoms as typical of keratoma senile. There have therefore been other cases which indicate that keratoma senile must by no means be considered to be a characteristic exclusively of senile degeneration of the skin. This view is corroborated in all respects by the case which has been reported, in which there were multiple efflorescences typical of keratoma senile in a young patient whose skin showed no trace of senile or presenile degeneration.

Apart from the remarkable manner in which the condition occurred, however, this case had still another very interesting significance for the genesis of these keratomas. If the youth of the patient was a remarkable fact, the age (5 years) at which the keratoma made its first appearance is still more important, the more so since the efflorescences displayed at various places a distinct systematization. On the strength of this it may be asked whether keratoma senile should not be regarded in such cases as a nevus change. Gans also considered this possibility in his cases and drew attention to the familial occurrence at an early age in his patients. In this connection an observation made by Unna,<sup>5</sup> who was able to demonstrate the presence of nevus cells in a keratoma senile, is also interesting. A publication by Lebenturier<sup>6</sup> and Dubreuilh who reported the familial occurrence of keratoma senile also points toward the nevogenic origin of this condition.

The case of keratoma senile which has been described here therefore furnishes a point of view which differs from the one generally held. I therefore feel justified in concluding with the support of certain statements found in the literature that keratoma senile may occur altogether independently of senile degeneration of the skin and that this dermatosis will probably have to be regarded in the future as a nevus condition. With regard to the usual lesions of senile keratosis which

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<sup>4</sup> Gans, O. *Histologie der Hautkrankheiten*. Berlin: Julius Springer, 1927, vol. 2, p. 374.

<sup>5</sup> Unna, P. G. cited by Gans.<sup>4</sup>

<sup>6</sup> Lebenturier. *Ann. de dermat. et syph.* 1896, p. 1038.

appear later in life, it is not likely that these differ essentially from those in the cases cited

On the basis of the case described I feel justified in proposing the term *keratosis praecancerosa* for *keratoma senile*. It is obvious that, as in Gans' cases, there is no question of senility. This term is also out of place in any case in which *keratoma senile* occurs at a comparatively early age (between 30 and 40 years). It therefore seems to me that since it is possible that there is no causal relationship between *keratoma senile* and senile degeneration of the skin, it is advisable to group all these conditions under the term *keratosis praecancerosa*, which disregards age and the characteristics of old age.

# PYODERMA GANGRAENOSUM

## A DEFICILNCY DISEASE COMPLEX

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The occurrence of ulcerations of the skin during the course of a debilitating disease has been a common observation but recently reports have been appearing in the dermatologic literature of an odd type of ulceration found usually in patients suffering from ulcerative colitis. Brunsting, Goeckerman and O'Leary<sup>1</sup> were the first to describe this condition fully. They reported five cases four of which were associated with ulcerative colitis. They gave the name of "pyoderma gangrenosum" to these ulcerations but in so doing emphasized the evident confusion in the nomenclature of the pyodermas. Pyodermas and ulcerations of the skin have been described under various names, such as ecthyma gangraenosum, gangrene due to the hemolytic streptococcus, infectious multiple gangrene, dermatitis gangraenosa, pyoderma chronica serpigiosa, amebiasis cutis and pyoderma chronica papillaris et ulcerans, all resembling each other in many respects with streptococci and staphylococci found in the lesions, but secondary to different general conditions and probably varying in their essential etiology. Lane and Stroud<sup>2</sup> pointed out that it is not unusual to note pyodermic infections in chronic diseases but the remissions and exacerbations of the cutaneous disorder do not follow so closely the respective variations of the primary disorder and the destruction of cutaneous tissue is not usually so marked as in pyoderma gangraenosum. In discussing the paper by Lane and Stroud Guy asserted that the association of ulcers in the skin and bowels and the other clinical findings constitute a definite clinical picture. In a study of the cases that have been described by Brunsting, Goeckerman and O'Leary<sup>1</sup> Lane and Stroud<sup>2</sup> McCarthy and Fields<sup>3</sup> Warner<sup>4</sup> Helmholz<sup>5</sup> Tischchenko and Krolezick<sup>6</sup>

1 Brunsting Louis A. Goeckerman William H. and O'Leary Paul A. Pyoderma (Ecthyma) Gangrenosum. Arch. Dermat. & Syph. **22** 655 (Oct.) 1930

2 Lane Clinton W. and Stroud Malone C. Pyoderma Gangrenosum. Arch. Dermat. & Syph. **27** 460 (March) 1933

3 McCarthy Lee and Fields Russel. Pyoderma Gangrenosa. New York State J. Med. **31** 801 (July 1) 1931

4 Warner W. P. A Case of Ulcerative Colitis in a Child Associated with a Bullous Skin Eruption. Canad. M. A. J. **18** 571 (May) 1928

and Glaubersohn,<sup>7</sup> it appears that generally a constant triad of symptoms is present—ulcerations of the bowels, ulcerations of the skin and hypochromic anemia—and that most of the patients are young girls. Whether these findings are indicative of a new symptom complex cannot yet be determined, owing to the fact that only a few cases have been described. Therefore, in view of the paucity of the literature, I wish to report the following case that shows the association of pyoderma gangraenosum with ulcerative colitis and to present a new theory concerning the essential etiology of the condition.

#### REPORT OF CASE

*History*—J. W., a white girl aged 12, was admitted to the children's ward of the York Hospital on March 13, 1932, in the service of Dr. Gibson Smith. Her chief complaints were frequency of bowel movements and a cutaneous infection on both ankles and both legs. With the exception of pertussis and measles she had been well and normal until September 1929, when after eating some veal, the patient and her mother and sister became acutely ill, with vomiting, diarrhea and abdominal cramps. Although her sister and mother recovered completely, the patient had not been well since then. There was continuous diarrhea, and blood and mucus were noted in the stools. In 1932 she first observed "sores" on her legs and later, following a bruise, her left ankle became infected, and an indolent ulcer developed. She entered the hospital, and after a month there returned home with the cutaneous condition improved but not completely healed and her stools still liquid. Two months afterward she was confined to bed for two weeks with polyarthritis, subsequently, milder attacks of arthritis and pains in the muscles were frequent. In the latter part of 1933 a large boil developed on the right leg, and soon "hundreds" of small pustules appeared over the legs, buttocks, the lower part of the abdomen and the arms. She reentered the hospital on Jan. 1, 1934, and has remained there to the present time. On admission she was found to be dehydrated, the stools were liquid and involuntary, and the lower and upper limbs were covered with various-sized confluent ulcerations. In about six months the ulcers healed and the stools were less frequent. In September 1934 the diarrhea again became more marked, and a large abscess developed on the dorsum of the left foot. A deep ulcer formed, the tissues seemed to melt away, and the edges of the ulcer overhung the rapidly sloughing substructure. Coincidentally, small pustules developed over the lower part of the legs and over the right arm. The pustules rapidly became confluent, forming large denuded areas almost encircling the calves and ankles. On the dorsum of the right foot the tendons were widely exposed. Six months after the onset of this acute exacerbation the ulcerations were healed, with the exception of a few small areas on the legs; the diarrhea was lessened, and the patient was able to sit in a wheel-chair.

At the admission in January 1934 a slight sinking of the bridge of the nose was noted, the cartilage and part of the bony septum had been absorbed, and an

5. Helmholtz, Henry F. Chronic Ulcerative Colitis in Childhood, *New York State J. Med.* **26** 46 (Jan. 15) 1926.

6. Tischnenko, A. and Kroiczik, H. Zur Frage der Pyoderma chronica serpigiosa, *Dermat. Ztschr.* **52** 11 (Feb.) 1928.

7. Glaubersohn, S. A. Pyoderma Chronica Ulcerosa, *Dermat. Wchnschr.* **88** 497 (April 6) 1929.

effect of saddle nose was produced. Also, stools were seen coming from the vagina, and a milk enema flowed from the vagina almost as soon as it was inserted in the rectum, undoubtedly as the result of a rectovaginal fistula.

Before the onset of her illness, in September 1929, she weighed 75 pounds (34 Kg), in April 1932 her weight was 64 pounds (29 Kg), in January 1934, 41 pounds (18.6 Kg), in September 1934, 58 pounds (26.3 Kg), and in March 1935, 48 pounds (21.8 Kg).

*Physical Examination* (March 1935)—The patient appeared five years younger than her actual age. She was thin, emaciated and pale. The skin had a slight brownish tint and was dry. No axillary or pubic hair was present. The irises reacted normally. The defect of the septum has been described. The dentition was normal for her age, and infected teeth had been removed. The tongue was smooth, pink



Fig 1—*A* appearance of the patient in December 1934 after the ulcerations were beginning to heal, with the formation of granulation tissue. *B* side view of the patient in December 1934, showing emaciation, nasal depression and encirclement of the leg by the ulcerations.

and glossy. The papillae were flat and no ulcerations were present. The thyroid was not enlarged. A soft systolic murmur was heard best at the base of the heart. The lungs were normal and showed no evidence of tuberculosis. No masses or areas of tenderness were palpable in the abdomen. The right arm showed areas of healed ulcerations with cicatricial contracture that prevented full extension. Both legs also showed healed ulcerations over the calves and ankles with moderate contractures. Touch, pain and temperature sensations were normal; the reflexes were present; coordination was good and there was no loss of muscular power other than would be expected from such a long debilitating sickness. The mentality was exceptionally good.

Throughout the course of the disease a low, irregular fever had been present which varied directly with the severity of the bowel movements and cutaneous changes

*Laboratory Examinations*—Examination of the stools made in January 1934 and on five subsequent dates showed no amebas or other parasites. Many leukocytes and erythrocytes and much mucus were always present. Cultures showed staphylococci, *Bacillus coli* and, on two occasions, *Bacillus pyocyaneus*. Efforts to isolate the diplococcus of *Bergen* were of no avail.

Cultures from the open cutaneous lesions showed a profuse growth of staphylococci on mediums used as a routine, and examination of material from an abscess area following phlebitis produced by an intravenous injection of dextrose, revealed a pure culture of *B. coli*.

A blood count taken in January 1934 revealed the following: red cells, 1,660,000; white cells, 9,080; hemoglobin content, 26 per cent; polymorphonuclears, 60 per



Fig. 2—Roentgenogram taken in January 1935, following a barium sulfate enema.

cent, small lymphocytes, 34 per cent, large lymphocytes, 3 per cent, myelocytes 2 per cent, eosinophils 1 per cent, reticulocytes, 1.5 per cent. In March 1934 the red cells numbered 2,540,000, and the hemoglobin content was 48 per cent. Subsequent counts have varied in this range, according to the severity of the symptoms and the treatment, particular improvement was noted following blood transfusions.

The results of two Wassermann and two Kahn tests of the blood were negative. The intradermal tuberculin reaction was negative twice. The blood calcium content was 10.7 mg per hundred cubic centimeters; the blood phosphorus content was 3.27 mg per hundred cubic centimeters. The gastric contents were normal, with no diminution of acid. The urine was normal, with occasional small traces of albumin.

Roentgen examination following a barium sulfate enema on Jan. 3, 1935, revealed a spastic irregularly filled terminal ascending colon. The transverse

colon exhibited loss of haustral markings, and the cecum was "ruddy" in appearance. The impression of Dr. L. S. Landis, the roentgenologist, was that the condition was ulcerative colitis.

Proctoscopic examination by Dr. W. F. Gemmill on Jan. 1, 1935, revealed the walls of the ampulla as granular and slightly edematous but not ulcerated. Above the lower valve there were many ulcers, elongated, sloughing and for the most part, parallel to the long axis of the bowel. Above this area much ulceration and contraction of the valve, with encroachment on the lumen, were seen.

*Treatment*—In the course of her illness the patient has been treated with nearly every remedy that has been suggested to alleviate her condition. An effort was made to ascertain the nature of her diet before the onset of the diarrhea and the impression was received that it was somewhat unbalanced with a lack of green vegetables and fruit and an overabundance of meat, potatoes, milk and pie. At the onset, before she came to the hospital, she was placed on a soft bland diet lacking essential vitamins and was given large doses of castor oil "to control her diarrhea." When she entered the hospital she was placed on a high caloric smooth diet and vitamins were given in the form of viosterol, a liver concentrate with iron cod liver oil and fruit juices. In spite of her negative reactions to blood tests and her good family history a course of neoarsphenamine and sulfarsphenamine was given, with poor results, tending to show that the saddle nose was due to pyogenic ulceration and not to syphilis. Likewise, emetine was tried, with the hope that latent amebiasis might be the underlying etiologic factor but this drug too failed. Ammonium chloride, calcium gluconate, belladonna, kaolin irrigations of the "bowel" with potassium permanganate and various other remedies were tried. Barger's serum or vaccine was not given on account of the negative results of examinations of the stool and because of the controversial opinions on its efficacy.

At the present time the stools are limited to three or four a day and the cutaneous lesions have practically healed. Whether this result is due to a remission or to the treatment is highly debatable but I believe that the following procedure has helped to relieve the patient: elimination of foci of infection particularly in the teeth, repeated blood transfusions, the intravenous administration of dextrose, feeding a high caloric, high vitamin diet and the administration of calcium. The diarrhea seemed best controlled by kaolin and often camphorated tincture of opium. U. S. P. was necessary. After various antiseptics and ointments were tried the best results in healing the cutaneous lesions were obtained by painting the lesions daily with acriflavine base in a 1:1500 solution and then applying irradiated petrolatum.

*Differential Diagnosis*—The common causes of ulcerations in the large bowel are tuberculosis, amebic colitis and idiopathic ulcerative colitis. The negative tuberculin reactions, the normal condition of the chest and the absence of the tubercle bacillus exclude the first. No amebas were found in repeated examinations of the stools and no history of intestation was elicited. The onset of the patient's illness occurring suddenly after the ingestion of veal with similar symptoms in other members of her family bespeaks an infectious origin. There is no question but that an infection was instrumental in originating the colitis but the continuance of the latter must be due to some factor peculiar to the patient herself. Portis<sup>8</sup> expressed the belief that nonspecific ulcerative colitis is nothing more than chronic bacillary dysentery with a superimposed secondary infection but it

<sup>8</sup> Portis, Sidney A.: Treatment of Ulcerative Conditions of Colon. *M. Clin. North America* 18:1319 (March) 1935.



is difficult to explain under that theory why the mother and sister should have recovered completely and why there was an absence of any contagiousness or infectiousness in the subsequent course. The results of proctoscopic examination, the changes revealed by the roentgen examination following the barium sulfate enema, the appearance and bacterial flora of the stools, the marked anemia and the long, intermittent course fall under the category of what is poorly named nonspecific ulcerative colitis. Pyoderma, which is a conspicuous feature in this case, has been found occasionally associated with ulcerative colitis and has been called pyoderma gangraenosum. It is my impression that the pyoderma is not secondary to the colitis but is another expression of a symptom complex of which the colitis, the anemia and the lack of cutaneous resistance to infection are merely parts. The latest conception that ulcerative colitis is an avitaminosis is worthy of careful consideration, particularly as the importance of cutaneous changes is noted in all states of vitamin deficiency. As Mackie and Pound<sup>9</sup> observed, it is seldom possible to elicit a history of dietary deficiency before the onset of the colitis, and it is possible that the patient's diet may have been deficient. However, after the onset, owing to an improper prescribed diet, forced purgation and improper absorption, there can be no doubt that she presented a prolific soil for the growth of a disorder due to vitamin deficiency. On admission to the hospital she presented the following characteristics of a deficiency state: a smooth tongue, a dry skin with brownish pigmentation, pyoderma and hypochromic anemia and the condition fully bears out Mackie's<sup>10</sup> conclusion that evidence of a deficiency state is observed in the majority of cases of ulcerative colitis, particularly those that find expression in the buccal and lingual mucosa, the skin, the type of anemia and the blood chemistry.

#### ETIOLOGY OF PYODERMA GANGRAENOSUM

The exact explanation of the mechanism underlying the formation of these ulcerations is still unsettled. McCarthy and Fields<sup>1</sup> considered the cutaneous changes in their case only a part of a generalized infection with consequent lowering of the resistance of the skin to bacterial invasion. Brunsting and his associates<sup>1</sup> discussed Meleney's work on symbiosis between staphylococci and streptococci and then suggested that allergy may play a part similar to the production of cutaneous lesions in syphilis, tuberculosis and iododerma. In this connection the work of Schwartzman<sup>11</sup> who produced hemorrhagic necrosis at the site of an intracutaneous injection of *Bacillus typhosus* in a rabbit after live cultures of streptococci were injected intravenously, is of great interest. Lane and Stroud<sup>2</sup> emphasized the predominance of a hemolytic *Staphylococcus albus* and a streptococcus in the lesions in their case and suggested a symbiotic relationship as the causal factor. However, neither

9 Mackie T. T., and Pound, R. E. Changes in the Gastro-Intestinal Tract in Deficiency States, *J. A. M. A.* **104** 613 (Feb. 23) 1935.

10 Mackie Thomas T. Ulcerative Colitis. II The Factor of Deficiency States, *J. A. M. A.* **104** 175 (Jan. 19) 1935.

11 Schwartzman G. The Phenomenon of Local Skin Reactivity to Streptococcus Hemolyticus-Scarlatinae, *J. Infect. Dis.* **48** 183 (Feb.) 1931.

allergy nor the lowered cutaneous resistance explains the remissions and exacerbations of the cutaneous lesions corresponding to the severity of the intestinal symptoms or why this condition does not occur more often in a number of other chronic debilitating conditions. In this case I believe that the same factor that produced the ulcerations in the bowel also produced the ulcerations in the skin and that the streptococci and staphylococci found in the cutaneous lesions were secondary invaders, just as staphylococci, the colon bacillus, Baigen's diplostreptococcus and many other organisms are secondary invaders in the lesions in the colon.

Since pyoderma gangraenosum is generally found in cases of ulcerative colitis, it is of interest to note the changing attitude of physicians toward that disease. After Baigen brought forth his conception that ulcerative colitis is of infectious origin and is due to a specific lancet-shaped, gram-positive diplococcus and that the infection is conveyed to the colon by repeated showers of bacteria that are thrown into the circulation from a distant focus, it was thought that the exact etiology of this disease was definitely established. But soon various papers appeared that questioned the specificity of Baigen's diplococcus. Rafsky and Manheims<sup>12</sup> found Baigen's organism in patients not suffering from ulcerative colitis and only twice in thirty cases of that disease in which proctoscopic examination was made. Nissen<sup>13</sup> likewise found the diplococcus in many patients not suffering from ulcerative colitis. Buttriaux and Sevin<sup>14</sup> thought that the disease is of infectious origin but stated that various organisms—the dysentery bacillus, the bacillus of Morgan, gonococci, streptococci, *Staphylococcus aureus* and the pneumobacillus as well as the diplococcus of Baigen, are of etiologic significance. Downing<sup>15</sup> reported a case of ulcerative colitis due to a different type of streptococcus and Bassler<sup>16</sup> demonstrated a diffuse ulceration of the colon due to the colon bacillus group which may develop intensely virulent strains under certain conditions. Bonorino Udaondo<sup>17</sup> expressed the belief that an infection is at the basis of this condition.

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12 Rafsky, Henry A. and Manheims, Perry I. The Significance of the Baigen Organism as an Etiologic Factor in Ulcerative Colitis, *Am J M Sc* **183** 252 (Feb.) 1932.

13 Nissen, Archibald H. Atomic Stasis. *M Clin North America* **13** 269 (July) 1929.

14 Buttriaux, R. and Sevin, A. On the Etiology of Ulcerative Colitis, *Ann Inst Pasteur* **17** 173 (Aug.) 1931.

15 Downing, Harold F. Report of a Case of Ulcerative Colitis Probably Due to Streptococcus Infection. *Arch Pediat* **45** 310 (May) 1928.

16 Bassler, A. Diseases of the Digestive System. Philadelphia F. A. Davis Company 1920 vol. 2.

17 Bonorino Udaondo, C. Etiology of Chronic Ulcerative Colitis, *Arch d anal de l'app digestif* **18** 1081 (Dec.) 1928.

but was uncertain whether a specific agent is the cause or whether various organisms are involved. He maintained that since there are so many bacteria in the intestinal tract, the finding of one type that predominates does not prove it to be the essential cause of a pathologic condition and that, furthermore, under certain conditions nonpathogenic organisms may become pathogenic. Brown and Paulson<sup>18</sup>, Heinze<sup>19</sup>, Tucker,<sup>20</sup> Streicher and Kaplan<sup>21</sup> and many other observers expressed their belief that Barga's organism is only one of many secondary invaders of the diseased colon and that the primary cause is still unknown. Torrey<sup>22</sup> noted, in discussing the etiologic significance of this diplococcus, that, as is true for streptococcal infections generally, it seems evident that the soil must be prepared by some preceding infectious or devitalizing condition. In the same vein of thought, Brown<sup>23</sup> asserted that the cause of ulcerative colitis is not to be found in the presence of a definite infective agent but rather in the absence of some protective substance or mechanism or something which normally inhibits the bacterial invasion of the intestinal wall, perhaps owing to metabolic error, endocrine disturbance, lack of a specific bacteriophage or lack of some normal bactericidal substance in the intestinal mucosa.

Since there is so much doubt as to the infectious nature of ulcerative colitis and particularly as to the essential etiologic significance of Barga's diplococcus, various investigators have been giving increasing attention to this problem and have considered in turn allergic, vagotonic, psychogenic, bacteriophagic and enzymatic factors. Recently many papers have appeared asserting that this debilitating disorder is due to vitamin deficiency. MacNaughton<sup>24</sup> early pointed out that Barga was more successful in producing ulcerative colitis in rabbits that had been fed a vitamin-free diet for ten days preceding the injection of his streptococcus, and Brown<sup>25</sup> stated that McCarrison's important experimental

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18 Brown, Thomas R., and Paulson, Moses. *Internat S Digest* **8** 67 (Aug) 1929

19 Heinze, Theodore E. *Ulcerative Colitis*, *M Clin North America* **17** 525 (Sept) 1933

20 Tucker, John. *Observations on Chronic Ulcerative Colitis*, *M Clin North America* **17** 1071 (Jan) 1934

21 Streicher, M. H., and Kaplan, B. *Chronic Ulcerative Colitis*, *I A M A* **94** 10 (Jan 4) 1930

22 Torrey, John C. *Symposium on Colitis (Bacteriology of the Human Colon with Particular Reference to Ulcerative Colitis)*, *Tr Am Gastro-Enterol A* **30** 129, 1928

23 Brown, Thomas R. *Some Observations in Chronic Ulcerative Colitis*, *Ann Clin Med* **4** 425 (Nov) 1925

24 MacNaughton, E. *Bacteriologic Studies in Chronic Ulcerative Colitis*, *Canad M A J* **18** 568 (May) 1928

25 Brown, Philip W. *Diagnosis and Treatment of Certain Types of Colitis and So-Called Colitis*, *M Clin North America* **16** 1333 (May) 1933

work, in which it was shown that an inadequate or deficient diet can so lower the functional protection of the gastro-intestinal tract as to impair its natural immunity to its normal inhabitants, could be applied to human beings. Hare<sup>26</sup> noted the resemblance of nonspecific colitis to a deficiency disorder and stated that both vitamin A and vitamin B are necessary for the development of a healthy mucous membrane in the intestine and for the retaining of its resistance against infection. Changes in the haustral markings and increase in the length of the colon were observed by Graham and Fletcher<sup>27</sup> in patients deprived of vitamin A, and Mackie<sup>10</sup> found evidence of a deficiency state in 62.6 per cent of seventy-five cases of ulcerative colitis. He stated that a deficiency is not to be regarded as an occasional complication of ulcerative colitis but probably constitutes an essential part of the underlying mechanism and suggested that the deficiency is multiple rather than single, with vitamins A, B<sub>1</sub>, B<sub>2</sub> and, possibly, D playing a rôle.

Whether ulcerative colitis shall be definitely placed among those diseases that are due primarily to a vitamin deficiency is still a moot question, but there can be no doubt but that as the disease progresses deficiency symptoms will be produced as Jones<sup>28</sup> stated owing either to an insufficient intake of a necessary ingredient of the diet, improper absorption or too rapid elimination. That abnormalities of the gastro-intestinal tract can play an important role in the causation of a deficiency disorder has been conclusively shown by Mettier and Minot<sup>29</sup>, Eusterman and O'Leary,<sup>30</sup> Castle, Heath, Strauss and Townsend<sup>31</sup>, Strauss and McDonald<sup>32</sup>, Friedenwald, Morrison and Morrison<sup>33</sup> and many other investigators. Loss of resistance to infection has been observed by

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26 Hare, D. C. Non-Specific Colitis in Relation to Deficiency Disorders and Anemia, *Brit. M. J.* **2**: 162 (July 28) 1934.

27 Graham, Duncan, and Fletcher, H. H. The Large Bowel in Chronic Arthritis, *Tr. A. Am. Physicians* **44**: 231, 1929.

28 Jones, Chester M. Peripheral Complications of Ulcerative Colitis, *M. Clin. North America* **16**: 7 (Jan.) 1933.

29 Mettier, S. R. and Minot, G. R. The Effect of Iron on Blood Formation as Influenced by Changing the Acidity of the Gastrointestinal Contents in Certain Cases of Anemia, *Am. J. M. Sc.* **181**: 25 (Jan.) 1931.

30 Eusterman, G. B. and O'Leary, P. A. Pellagra Secondary to Benign and Carcinomatous Lesions and Dysfunction of the Gastro-Intestinal Tract, *Arch. Int. Med.* **47**: 633 (April) 1931.

31 Castle, W. B., Heath, C. W., Strauss, M. B. and Townsend, W. C. The Relationship of Disorders of the Digestive Tract to Anemia, *I. A. M. A.* **97**: 904 (Sept. 26) 1931.

32 Strauss, M. B. and McDonald, W. A. Polynuritis of Pregnancy—A Dietary Deficiency Disorder, *I. A. M. A.* **100**: 1320 (April 29) 1933.

33 Friedenwald, I., Morrison, T. H. and Morrison, S. Modern Conception Concerning Certain Gastric Affections, *Internat. Digest* **26**: 53 (Jan.) 1935.

Clausen <sup>34</sup> in experiments on animals in cases of deficiency of vitamins A and C and with some degree of certainty in cases of deficiency of vitamin B. Thus, in ulcerative colitis a vicious cycle is instituted in which the lack of vitamins produces an increased infection with greater structural changes and consequently poorer absorption of vitamins.

Changes in the skin have been commonly noted in the established deficiency diseases such as pellagra, nontropical sprue, beriberi and xerophthalmia. An insufficient intake of vitamin A produces cutaneous changes, and Frazier and Hu <sup>35</sup> demonstrated that furunculosis, coming in the category of pustulation or pyoderma, is one of the common sequelae of xerophthalmia. Loewenthal <sup>36</sup> in discussing the dermal manifestations of vitamin A deficiency, stated that the infections that occur are due to breaches in the epithelial surfaces permitting a more than normal invasion of bacteria with which the body's normal defenses are unable to cope. He pointed out that there is no lack of an anti-infective factor and quoted Hennessey who found that the formation of leukocytes, bacteriolysins and precipitins continues normally in spite of avitaminosis. Keil and Scheer <sup>37</sup> described two cases of vitamin A and C deficiency in which follicular lesions occurred, and Morawitz <sup>38</sup> reported a case of chronic enterocolitis in which scurvy developed with the appearance of cutaneous changes. Sweitzer <sup>39</sup> found cutaneous manifestations to be present in xerophthalmia, scurvy, xanthosis and pellagra and emphasized the importance of vitamins A and G in keeping the skin normal. Wise and Sulzberger <sup>40</sup> expressed the belief that there may be many states of preavitaminosis which may furnish the soil for the development of dermatologic and other disease processes. Not only a one-sided diet but also inadequate absorption or utilization of the vitamins ingested may lead to such states. Mackie <sup>41</sup> described a case of nontropical sprue

34 Clausen, S. W. *Nutrition and Infection*, J. A. M. A **104** 793 (March 9) 1935.

35 Frazier, C. N. and Hu, Ch'uan-K'uei. *Cutaneous Lesions Associated with a Deficiency in Vitamin A in Man*, Arch. Int. Med. **48** 507 (Sept.) 1931.

36 Loewenthal, L. J. A. *A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency*, Arch. Dermat. & Syph. **28** 700 (Nov.) 1933.

37 Scheer, Max, and Keil, Harry. *Follicular Lesions in Vitamin A and C Deficiencies*, Arch. Dermat. & Syph. **30** 177 (Aug.) 1934.

38 Morawitz, P. *Pathologic Pigmentation of Skin and "Pigment and Vitamins,"* Klin. Wchnschr. **13** 324 (March 3) 1934.

39 Sweitzer, S. E. *Skin Manifestations of Avitaminosis*, Minnesota Med. **16** 670 (Nov.) 1933.

40 Wise, Fred, and Sulzberger, Marion B. *Editorial: The 1934 Year Book of Dermatology and Syphilology*, Chicago, The Year Book Publishers, Inc., 1934, p. 206.

41 Mackie, Thomas T. *Nontropical Sprue*, M. Clin. North America **17** 165 (July) 1933.

with a long chronic and remittent course severe diarrhea and pyodermic changes in the skin

In consideration of the facts that a vitamin deficiency is produced in ulcerative colitis and that lack of certain vitamins in the skin has been shown to produce cutaneous changes, I have come to believe that in my case of pyoderma gangraenosum the condition resulted from the lack of vitamins in the skin and bowels, permitting invasion by their usual bacterial inhabitants. I feel that feeding a high vitamin diet and the application of irradiated petrolatum to the lesions in the skin have materially helped the patient but that a cure is rather uncertain and I can explain this ineffectiveness as Cowgill<sup>42</sup> explained why the administration of vitamin B does not always cure beriberi when he brought out the following points: (1) A complicated rather than a single deficiency may be in part responsible for this result, and (2) even in experimental beriberi in animals this condition may occur through failure of the vitamin given by mouth to reach the most vitally situated lesions, on account of gastro-enteric disturbances. In this case the roentgenogram showed such malformation and distortion of the intestines that it is no wonder that the necessary vitamin cannot be absorbed just as arsphenamine can cure syphilis but has little or no effect on the structural changes that occur in the aorta or the myocardium. Turner<sup>43</sup> also brought out that the poor showing of vitamin therapy in pellagra may either be used as an argument against the specificity of vitamin G or may be interpreted as indicating that changes have taken place due to pellagra or some other disease or constitutional state which makes the vitamin ineffective.

#### SUMMARY

I feel that in my case the marked ulcerations of the skin and the bowel, the smooth atrophic tongue, the hypochromic anemia, the long intermittent course and the lack of any evidence of contagiousness suggest a deficiency disorder. The fact that the patient was not cured by vitamin therapy can be ascribed to the destruction of the absorptive mechanism in her intestinal tract and, to the complexity of the involved vitamins. I believe that cases of pyoderma gangraenosum are more common than the literature would lead one to believe that particular attention should be given to the skin of any patient suffering from long continued diarrhea and that it is essential that a high vitamin diet, liver extract, iron and calcium be given early in the course of such a condition. The final word on the etiology of pyoderma gangraenosum

<sup>42</sup> Cowgill, George R. Vitamin B<sub>1</sub> in Relation to the Clinic. *J. A. M. A.* 98:2282 (June 25) 1932.

<sup>43</sup> Turner, R. H. cited by Underhill, Frank P. Clinical Aspects of Vitamin G Deficiency. *J. A. M. A.* 99:120 (July 9) 1932.

and ulcerative colitis remains for the future to supply, but it is my opinion that this condition is not of an infectious nature but is due to the lack of some protective substance or vitamin in the skin and intestinal tract

#### CONCLUSIONS

A case of pyoderma gangraenosum occurring with ulcerative colitis is described

Marked evidence of a deficiency disorder was observed and it is believed that the changes in the skin were due to an avitaminosis

The occurrence of ulcerations in the skin and bowels in young girls with hypochromic anemia suggests a new symptom complex

142 East Market Street

# NATURE AND DISTRIBUTION ACCORDING TO AGE OF CUTANEOUS MANIFESTATIONS OF VITAMIN A DEFICIENCY

A STUDY OF TWO HUNDRED AND SEVEN CASES

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The classic manifestations of a deficiency of vitamin A in man, xerophthalmia and keratomalacia, have until recently been recognized as the only external lesions of this nutritional disorder. The failure of nutrition underlying such conditions is due either to an inadequate amount of the vitamin in the diet or to disease or functional derangements interfering with the utilization of this substance by the body. The relationship of the ocular changes to a deficiency of vitamin A has been established by frequent clinical and experimental observations in man and in laboratory animals.

The specific effect of a diet inadequate only in vitamin A is a keratinizing metaplasia of epithelium in many regions of the body, which is thought to be a phenomenon of repair stimulated by atrophy of the original epithelium. The replacement of normal epithelium by stratified keratinizing epithelium, similar to that of the normal epidermis, produces extensive visceral lesions in man and in animals, owing to the occlusion of ducts by desquamated keratinized cells and the consequent formation of cysts<sup>1</sup>. These effects were observed in man before keratinization of the conjunctival and corneal epithelium, which results in the development of xerophthalmia and keratomalacia<sup>2</sup>. From the recognition of the latter there is developing a broader conception of the clinical aspects of vitamin A deficiency. The disease can no longer

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1. Mori S. The Changes in the Para-Ocular Glands Which Follow the Administration of Diets Low in Fat-Soluble A, with Notes of the Effect of the Same Diets on the Salivary Glands and the Mucosa of the Larynx and Trachea, *Bull. Johns Hopkins Hosp.* **33**: 357 (Oct.) 1922. Wolbach S. B., and Howe, P. R. Tissue Changes Following Deprivation of Fat-Soluble A Vitamin. *J. Exper. Med.* **42**: 753 (Dec.) 1925. Goldblatt H. and Benischek M. Vitamin A Deficiency and Metaplasia. *ibid.* **46**: 699 (Nov.) 1927.

2. Blackman K. D. and Wolbach S. B. Vitamin A Deficiency in Infants. A Clinical and Pathological Study. *J. Pediat.* **3**: 679 (Nov.) 1933.



be thought of as local, affecting only the ocular tissues. Composed of a variety of epithelial structures, it is not surprising that the skin should be among the many tissues affected by this disease.

Among the early clinical descriptions of xerophthalmia minor changes in the skin were reported in association with the ocular condition in infants and young children. In 1883, de Gouvêa<sup>3</sup> writing on this subject, mentioned the dry and scurfy appearance of the skin of undernourished Negro children on the coffee plantations of Brazil. Bloch,<sup>4</sup> who first stressed the importance of vitamin A to xerophthalmia on the basis of clinical observations, described a dry, shriveled and scaly condition of the skin of infants affected by the disease. In more recent years a similar condition was described by Wilson and DuBois<sup>5</sup> and by Blackfan and Wolbach.<sup>2</sup> Opinions as to the significance of dryness of the skin occurring in these cases differ. Some have expressed the opinion that it is due more directly to dehydration, undernutrition and coexisting generalized infection than to the effect of any specific nutritional deficiency.<sup>2</sup> Those who expressed this opinion based it on the absence of changes in the structure of the skin characteristic of vitamin A deficiency.

#### FOLLICULAR HYPERKERATOSIS OF THE SKIN IN ADULTS

It is of importance to an understanding of the relationship of the cutaneous abnormalities to vitamin A deficiency to bear in mind that until recently most of the clinical observations were made on infants and children. Although xerophthalmia and keratomalacia were known to occur in adults, a study of the disease in a large number of adults was not available until Pillat<sup>6</sup> working at the Peiping Union Medical College, reported the results of his observations on a series of patients in a military camp near Peiping during the winter of 1929. Among 3 000 soldiers he observed 209 men ranging in age from 17 to 36 years with various ocular manifestations of vitamin A deficiency. Many presented signs of systemic disease including certain abnormalities of the skin, which Pillat thought were caused by a deficiency of vitamin A.

3 de Gouvea, H. Beiträge zur Kenntnis der Hemeralopie und Xerophthalmie aus Ernährungsstörungen, *Arch f Ophth* **29** 167, 1883.

4 Bloch, C. E. Lidelser hos småbørn opstaaet paa grund af fedtmangel. Xerophthalmia et dystrophia adipogenetica, *Ugesk f læger* **79** 349 1917, *abstr J A M A* **68** 1516 (May 19) 1917.

5 Wilson, J. R., and DuBois, R. O. Report of a Fatal Case of Keratomalacia in an Infant, with Postmortem Examination, *Am J Dis Child* **26** 431 (Nov) 1923.

6 Pillat, A. The Frequency of Deficiency Diseases of the Eye Due to Lack of Vitamin A in a Military Camp North of Peiping, *Nat M J China* **15** 585 (Oct) 1929, Does Keratomalacia Exist in Adults? *Arch Ophth* **2** 256 (Sept) 399 (Oct) 1929.

Fifteen of the patients, all with typical keratomalacia and without signs of deficiency of other vitamins, were studied by us with respect to the cutaneous lesions.<sup>7</sup> The results of this study were first reported at the Eighth International Congress of Dermatologists and Syphilologists at Copenhagen in 1930.<sup>8</sup>

The frequency with which the skin was involved among the many persons observed, the uniformity of the eruption and its response to dietary therapy led us to the conclusion that the cutaneous abnormalities were of more than coincidental significance. This conception was given further support by the nature of the minute changes in the skin, which were interpreted as analogous to those occurring in the tissues of the eye and other organs of animals and of man following deprivation of vitamin A.

*Effect of Diet*—The age of the 15 patients ranged from 19 to 33 years, the majority being in the early part of the third decade of life. The patients had lived for periods of from six months to one or more years on a diet consisting chiefly of rice, maize, millet, occasionally a poor grade of wheat flour, white cabbage and salted vegetables. Meat, eggs and green vegetables were rarely eaten. A few patients never had these foods and the others had them not more often than once a month.

The ordinary diet of middle-class Chinese in Peiping is normally below the optimum in proteins and in vitamins A and D and low in calcium and phosphorus.<sup>9</sup> Vitamins B and C are probably present in adequate amounts. The intake of fat is low, and the consumption of carbohydrate is relatively high. Practically all the fats and oils used for dietary purposes are of vegetable origin, and the fact that they are repeatedly heated in the open air may account for the destruction by oxidation of the relatively small amount of vitamin A they contain. Milk, butter and other dairy products are almost never used by the Chinese.

*Character of the Cutaneous Eruption*—As a group the patients showed a distinctive cutaneous eruption of uniform character, which, according to the history, usually preceded the onset of ocular symptoms. At first the skin became dry and slightly rough. The eruptive lesions appeared rather suddenly in a localized area of the body. They extended

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7 Frazier, C. N. and Hu, C. K. Cutaneous Lesions Associated with a Deficiency in Vitamin A in Man. *Arch. Int. Med.* **48**: 507 (Sept.) 1931.

8 Frazier, C. N., and Hu, C. K. Cutaneous Lesions Associated with Vitamin A Deficiency in Man, *Compt. rend. Cong. Internat. de dermat. et de syph.*, 1930, p. 482.

9 Wu, H., and Wu, D. Y. Study of Diets in Peking, *Chinese J. Physiol.* (suppl.) no. 1 July 1928, p. 135.

as a rule, with considerable rapidity, first involving the anterolateral aspect of the thighs or the posterolateral aspect of the upper part of the forearms. The eruption then spread to the extensor surface of both the upper and the lower extremities, the shoulders, the abdomen, the back and the buttocks and finally reached the face and the posterior aspect of the neck. The hands and feet were not involved, and only rarely were there lesions on the median portion of the thoracic region or in the axillary and genito-anal areas. In some patients the skin was generally darker than normal, and in a few it had a dull slate color. There was frequently absence of sensible sweating. The articular

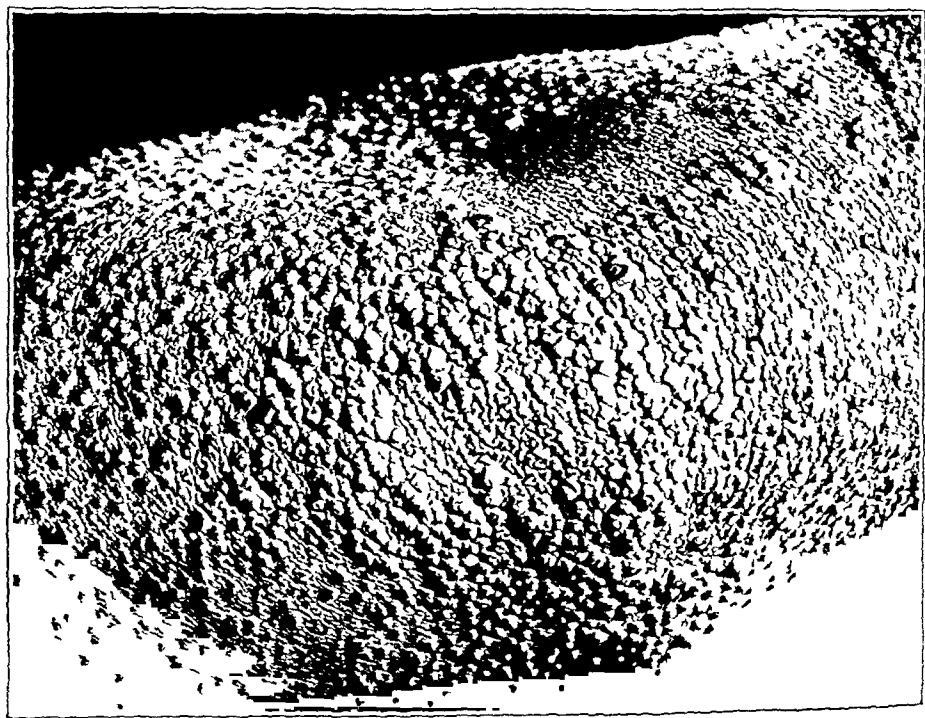


Fig 1—Follicular papules with central horny spines, showing various degrees of perifollicular infiltration, after a duration of three months. The cutaneous lesions were the only sign of vitamin A deficiency. The photograph is of natural size and of the region of the elbow.

folds lost their normal moisture, were dry and occasionally were covered with delicate scales. The normal surface markings were exaggerated in places, giving the skin a finely wrinkled appearance.

Distributed symmetrically the eruption was generally profuse, although in some cases it remained localized, for example, on the face or the neck. The eruption was distinguished by hyperkeratosis especially of the hair follicles in the form of dry, firm, pigmented papules containing a central intrafollicular keratotic plug. Many of these plugs projected from the hair follicles as horny spines or were

covered with a loosely adherent scale which bridged the occluded follicle. When expressed, the plugs left gaping cavities. The more recently formed papules tended to be conical, but as the degree of perifollicular infiltration increased they became hemispherical in some of the more severe cases.

On the face the eruption resembled acne due to the presence of many large comedones but differed from acne in respect to the dryness of the skin, which in common with the general tegumentary surface displayed a loss of secretory function. The lesions on the face were only rarely pustular.

The hair of the scalp and the nails were not remarkably affected. On the trunk and extremities the hair, which in the Chinese race is scanty and but little developed, was less apparent than normal, owing to the occlusion of the follicles and consequent atrophy. The scalp was slightly scaly in some cases.

*Effect of Dietary Treatment*—The course of the eruption was modified by dietary treatment. After the patients were admitted to the hospital, they were given a well balanced diet and cod liver oil. The cutaneous lesions gradually subsided along with the lesions of the eyes. The response, however, was much slower, from two to three months was required for the skin to regain its normal texture, whereas the healing of the ocular lesions was usually complete within a month. An improvement in the secretory function of the skin was apparent much sooner, visible sweating in some cases being established after two weeks of treatment. When the eruptive lesions disappeared delicate atrophic scars surrounded by a zone of hyperpigmentation remained at the site of the follicular orifices.

Although the therapeutic test in these cases was not discriminating as between a lack of vitamin A and a lack of other elements in the diet it nevertheless demonstrated that the lesions of the skin responded to dietary treatment which insured an adequate intake of vitamin A. During the period of observation no medicament was applied directly to the skin, and baths were limited to one a week. It is also to be noted that none of the patients presented clinical signs of disease caused by a deficiency of other vitamins.

More satisfactory proof of the specific effect of treatment was provided recently by the work of Loewenthal<sup>10</sup> in East Africa. Among 81 prisoners in whom night blindness and xerophthalmia developed during imprisonment, 74 also had a cutaneous eruption similar to that observed in the patients in Peiping. Without modifying the diet on which the prisoners were subsisting at the time the signs of

<sup>10</sup> Loewenthal I. I. A. A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency. Arch. Dermat. & Syph. 28:700 (Nov.) 1933.

vitamin A deficiency appeared, 30 cc of cod liver oil was given daily to each man over a period of nine weeks. At the end of this time night blindness and xerophthalmia had disappeared in every case and the cutaneous eruption in more than 98 per cent of those affected. As there is no reason for attributing the curative effect of cod liver oil in these cases to other than its vitamin A content, the results are especially significant.

More significant, however, were the results obtained by Loewenthal in 2 patients treated with an extract containing only vitamin A. In both xerophthalmia and night blindness cleared up quickly. In 1 patient the dermatosis completely disappeared in eight weeks, and in the other it had almost disappeared in seven weeks, when the supply of the extract was exhausted.

*Geographic Distribution*—During the five years since the first cases of the cutaneous disorder were studied in Peiping, the condition has been observed not only here but in other localities in China and in widely scattered parts of the world. The most significant observations are those of Loewenthal in East Africa which have previously been referred to. Nicholls<sup>11</sup> in Ceylon observed similar abnormalities of the skin and xerophthalmia, among other conditions, developing in a large group of prisoners living on a very poor diet. Many of the prisoners also had mild neuritis and diarrhea or dysentery. Nicholls attributed the disease primarily to vitamin A deficiency but thought that the lack of other food factors was also responsible, especially a lack of vitamin B. A single case was reported by Goodwin<sup>12</sup> in London which is of interest because the patient did not present ocular disturbances except pigmentation of the conjunctiva. Two cases were described by Scheer and Keil<sup>13</sup> in New York. The interpretation of the cutaneous eruption was confused by the presence of coexisting manifestations of scurvy, which the authors considered an etiologic factor in the production of the follicular lesions.

At the meeting of the Far Eastern Association of Tropical Medicine in Nanking in October 1934, when this subject was discussed<sup>14</sup> conversations with Rosedale from Singapore and Wright from Madras seemed to indicate that cutaneous involvement may be a much more frequent manifestation of vitamin A deficiency than has hitherto been recognized.

11 Nicholls, L. Phrynoderma. A Condition Due to Vitamin Deficiency, *Indian M. Gaz.* **68** 681 (Dec.) 1933.

12 Goodwin, G. P. A Cutaneous Manifestation of Vitamin A Deficiency. *Brit. M. J.* **2** 113 (July 21) 1934.

13 Scheer, M., and Keil, H. Follicular Lesions in Vitamin A and C Deficiencies, *Arch. Dermat. & Syph.* **30** 177 (Aug.) 1934.

14 Frazier, C. N., and Hu, C. K. The Cutaneous Manifestations of Vitamin A Deficiency in Man, *Far East. A. Trop. Med., Tr. Ninth Cong.* **1** 461, 1934.

## FOLLICULAR DERMATOSIS IN PATIENTS WITH XEROPHTHALMIA

Since the occurrence of the disease in what may be described as an epidemic form in the year 1929, patients with both the ocular and the cutaneous manifestations of vitamin A deficiency have been observed with some frequency in Peiping. Among 18 cases observed during this time, the course of the disease, the clinical and histologic characteristics of the eruption and the response to dietary therapy have uniformly corresponded with the original observations. All the patients were males, ranging in age from 14 to 31 years, with 2 exceptions. These were children 4 and 5 years of age, respectively. By occupation, 8 were apprentices to various trades, 3 were soldiers, 2 were wards of an orphanage, 3 were small tradesmen and the remaining 2 were unemployed children. They gave histories of having lived on inadequate diets for from two to five years prior to the onset of symptoms. The diet of 12 of the patients consisted almost entirely of cereals, such as corn, wheat and millet and white cabbage and salted vegetables. In 1 case signs of vitamin deficiency appeared subsequent to an attack of bacillary dysentery.

At the time of admission to the hospital ocular symptoms had been present for from one to nine weeks. One patient gave a history of recurrent attacks of visual impairment over a period of one and a half years. These began a few months after the patient became an apprentice in a rug factory, where he was provided with food of very poor quality. Another patient with a severe cutaneous eruption, presented only the corneal scars of acute ophthalmia, which had occurred four months prior to his admission to the hospital. The patient also had cystitis with many epithelial cells in the urine, a chronic productive cough without bacteriologic or roentgenologic evidence of pulmonary tuberculosis and diarrhea of one month's duration. Many epithelial and pus cells were found in the stools, but ova, parasites or pathogenic microorganisms were not present. Although the patient was not observed long enough to determine the effect of dietary therapy, it seems not unlikely that the various clinical manifestations may have had a common etiologic origin.

The duration of the cutaneous eruption with respect to the onset of xerophthalmia varied considerably among the 18 patients. In 1 case ocular and cutaneous lesions developed simultaneously one month before he was admitted to the hospital. In 9 cases from two to four months intervened between the appearance of the eruption and the onset of ophthalmia and in 3 cases the eruption had been present for six months and preceded the onset of keratomalacia by as long as five months.

The individual records of the cases of 2 patients from this group are reported here for the purpose of more clearly showing the character-

istic features of the history and course of the disease than is possible in a general discussion

#### REPORT OF CASE

**CASE 1—History**—A Chinese youth 17 years of age was admitted to the hospital on Nov 5, 1932, complaining of a cutaneous eruption, night blindness and blurring of vision

The patient first noticed a patch of rough skin in the flexure of the joint of the right elbow four months before he was admitted to the hospital. On the following day a similar condition was noted on both anterior axillary folds and within four days the eruption became generalized. There was no itching, pain or tenderness. The patient complained, however, of a sense of extreme dryness over the entire body. Three months after the eruption appeared he noticed that he could not see with his left eye in the evening after the lights were on. A few days later blurring of vision occurred, and this gradually increased in severity up to the time he was admitted to the hospital. The right eye became involved in a like manner twenty days before he came to the hospital.

**Diet**—The patient had two meals a day, consisting of corn bread, sweet potatoes, white cabbage and salted carrots. He did not eat meat, fish or eggs.

**Physical Examination**—The patient was underdeveloped and undernourished. There was generalized hyperkeratosis of the hair follicles, affecting all regions except the scalp, palms and soles. Only a few papules were present in the sternal region. The skin was very dry and without signs of sweating even in the axillary and genital regions. The hair was dry and dull. The nails were normal. There was no hyperpigmentation of the skin.

The nasal mucosa was covered with crusts. The uvula was red and edematous, and the throat was slightly injected.

The eyelids were inflamed and scaly at the margins. The palpebral conjunctiva was blurred by moderate papillary hypertrophy, and the bulbar conjunctiva showed ciliary congestion. The right cornea was moderately vascularized at the upper segment and infiltrated and ulcerated at the lower segment. There were deep infiltration and a perforated ulcer at the lower outer quadrant of the left cornea. Scrapings from the bulbar conjunctiva contained a few xerosis bacilli. Histologic examination of a section of conjunctiva from the lower fornix showed moderate hyperpigmentation of the type found in cases of vitamin A deficiency.<sup>1</sup> There were no other abnormal physical findings. The lungs were normal on roentgen examination.

**Laboratory Examination**—The urine contained a few epithelial cells. There were 4,570,000 erythrocytes per cubic millimeter of blood, with a hemoglobin content of 94 per cent. The white cell count was 8,450 per cubic millimeter. The Wassermann and Kahn reactions were negative. The stools contained ova of *Ascaris* and hookworm. The basal metabolic rate was  $-4.9$ . The blood plasma contained albumin, 2.95 per cent, globulin, 2.25 per cent, and euglobulin, 0.21 per cent. The cholesterol content was 60 mg, the inorganic calcium content, 10.6 mg, and the phosphorus content, 5 mg per hundred cubic centimeters of blood. Gastric acidity was normal.

**Course and Treatment**—The patient was given a balanced diet and 30 cc of cod liver oil daily. Baths were not permitted and he was kept out of

15 Mori S. The Pathology of the Pigmentation of Bulbar Conjunctiva in Xerosis Epithelialis Conjunctivae. *J Orient Med* 2:103 (Feb) 1934.

bed most of the day. After ten days, slight moisture was detectable on the nose, in the sternal region and in the popliteal spaces. The genitalia did not seem to be so dry, but the axillary spaces remained as dry as when the patient was admitted to the hospital. The condition in the eye was much improved by the sixteenth day in the hospital. Dark adaptation was normal. The bulbar conjunctiva was lustrous, and the corneal ulcer was healing. Thirty-two days after the patient was admitted to the hospital the sweat glands functioned normally, and there was beginning, although slight, improvement of the skin. At this time the administration of cod liver oil was discontinued, and carotene, 0.001 Gm., was injected subcutaneously twice a day. In two weeks most of the keratotic papules had exfoliated, and the eyes were normal except for the scars of the corneal ulcer. At the time the patient was discharged, after sixty-five days in the hospital, most of the cutaneous lesions had disappeared, leaving pigmented, slightly depressed scars at the opening of the involved hair follicles. When examined after three months, the skin was still xerotic in places. During this interim, the patient, according to his own statement, had been taking 30 cc of cod liver oil daily.

*Comment*—In this case the response of the eruption to dietary treatment coincided with the healing of the ocular lesions. The eruption was one of the most profuse and well developed that we observed. After the substitution of carotene for cod liver oil it was thought that the therapeutic response was more rapid. During the first month of observation no very striking improvement in the condition of the skin was apparent, although the ocular lesions underwent prompt regression to almost complete healing before carotene was administered.

The reappearance of moisture in the folds of the large joints and around the genitalia was the first sign of improvement and it occurred earlier than any detectable change in the eyes. The fact that the sweat glands became active before there was any exfoliation of cornified material and clearance of the openings of the sweat ducts is strongly suggestive of a primary failure in secretory function preceding the mechanical occlusion of the ducts. The early appearance of moisture on the surface was also observed in other patients and constitutes one of the first signs of recovery from the effects of vitamin A deficiency.

*CASE 2—History*—A Chinese student 14 years of age was first seen on Feb. 1, 1934. He complained of a symptomless eruption, sore eyes and a dry cough.

About four months before the patient was admitted to the hospital he noted many dark, pointed granules on the back of each hand. These became more numerous and prominent and rapidly spread to the extensor surfaces of the arms. Gradually the lower extremities became involved. About one month after the onset of the eruption the face and neck became dark and covered with many filamentous projections. Three months after the first cutaneous lesions were noted the eyes became red and lacrimation was profuse. Night blindness and blurring of vision were not present. After a week or more there developed a nasal obstruction, a dry cough and subsequently hoarseness. There had been no loss of weight. The patient had not felt ill at any time during the course of the disease.



Since early childhood, the patient's health had been robust, and he had always lived in fair economic circumstances. The other members of the family were in good health.

*Diet*—For a period of four years the patient's diet consisted almost entirely of cereals and cabbage, occasionally some green vegetables and one or two eggs a week. After witnessing the slaughter of an ox he had not been able to relish meat of any kind and refused to eat it.

*Physical Examination*—The patient was well developed and looked well nourished. He had an occasional nonproductive cough. The hair was clipped short, showing a normal scalp. The face was flushed, except for a yellowish

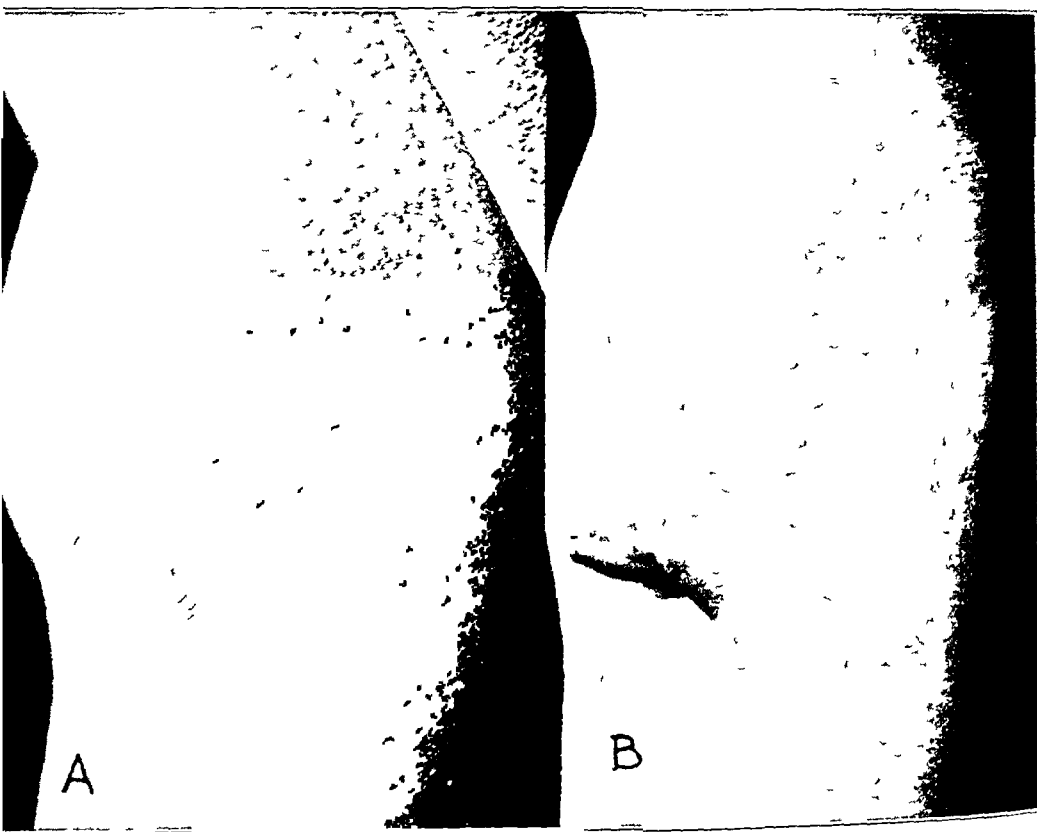


Fig 2 (case 2) —A shows generalized xeroderma and follicular hyperkeratosis associated with xerophthalmia. B shows the effect of five weeks of dietary and halibut liver oil therapy.

pallor around the nose and mouth. Covering the face, except in the nasolabial region, were innumerable fine keratinous filaments projecting from 1 to 3 mm above the surface and giving the cheeks the appearance and feel of velvet. Filiform processes were also scattered irregularly over the trunk and extremities. These were intermingled with many dry conical papules containing central horny masses. Either the papules were covered by a hard, dark colored scale or the central plugs projected spine-like from the summit of the papule. The entire cutaneous surface had the appearance of highly accentuated goose flesh. Between the papules the skin was dry and hyperpigmented. The buttocks were a

mass of horny papules (fig 2A) On the palms were a few hyperkeratotic patches, irregular in shape and without a discrete papular formation Keratinous spines or plugs were not present in these places Over the knuckles and around the heels and ankles were elevated, coarse, hyperkeratotic plaques of a warty appearance (fig 3A) These were from 1 to 2 cm in diameter At no place was there any redness or swelling of the skin There were many filiform lesions on the prepuce and on the scrotum The axillae and soles were dry but without sign of papular formation

The eyelids were moist and red, and there was mild inflammation of the meibomian glands of one lid The palpebral conjunctiva of both eyes showed papillary hypertrophy and slight pigmentation of the lower lid There were pale, triangular xerotic spots (Bitot's spots) on both the temporal and the nasal side of the bulbar conjunctiva adjacent to the limbus These were only faintly visible The cornea of each eye was clear, but at the limbus there was a faint pannus Adaptation to darkness was 4/9 The vision was normal

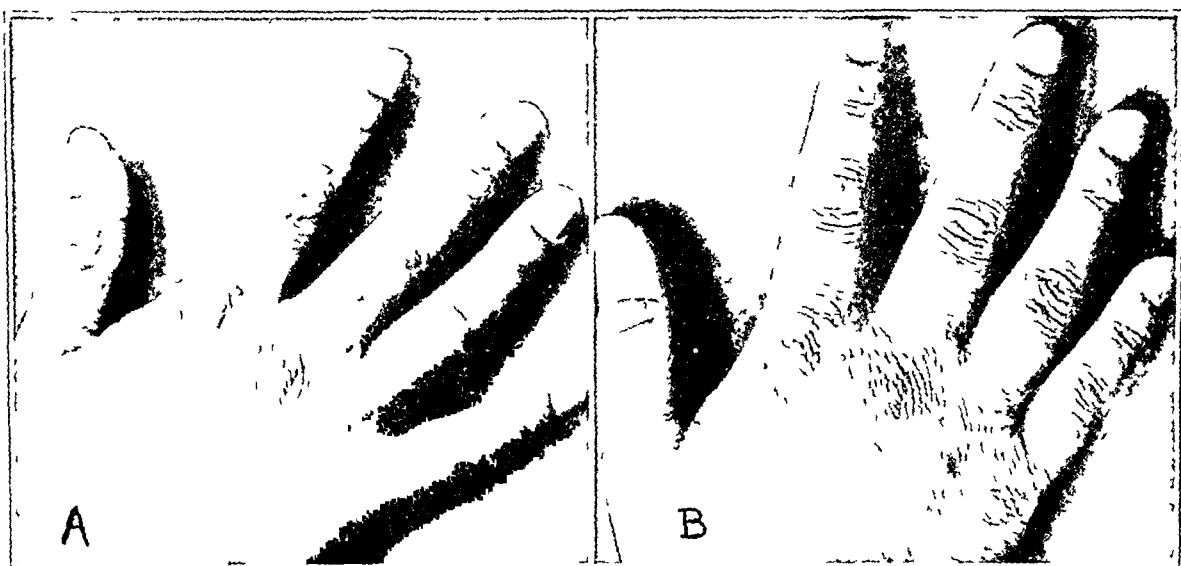


Fig 3 (case 2) — *A* shows hyperkeratotic plaques of four months' duration, with generalized follicular keratosis and xerophthalmia *B* shows the effect of dietary treatment over a period of one month

A dry, purulent discharge adhered to the nasal mucosa The tongue was slightly coated, and prominent red papillae stood out over the anterior one third of its surface The pharyngeal mucosa was moderately congested, and the voice was hoarse

The lungs, heart and abdomen were normal There was no edema of the extremities or tenderness of the muscles of the calves The neurologic examination revealed nothing abnormal The temperature was normal

*Laboratory Examination*—The urine contained an occasional epithelial cell The red blood cell count was 4,250,000 per cubic millimeter with a hemoglobin content of 137 Gm per hundred cubic centimeters There were 9,500 white cells per cubic millimeter and the differential count was normal The inorganic calcium content of the blood was 9.8 mg, the phosphorus content 3.9 mg, and the nonprotein nitrogen content of the plasma, 18 mg, per hundred cubic centimeters The value for albumin was 3.13 per cent, and that for globulin, 2.16 per cent The

Wassermann and Kahn reactions of the blood were negative. The stools did not contain ova or parasites.

*Course and Treatment*—A full hospital diet, containing liver, and 10 drops of halibut liver oil were given the patient daily. After two weeks the eyes were normal, and most of the filamentous processes had disappeared from the face. The forehead, which had felt like sandpaper, was smooth. During this time no local medication was used, and a bath was given only once a week. Thirty-five days after the patient was admitted to the hospital the skin over the buttocks and extremities was relatively smooth, and the horny plaques on the knuckles had disappeared (figs 2 B and 3 B). A few remnants of papules and hyperpigmentation around the hair follicles were present forty-two days after treatment was commenced. The erythrocyte count had increased to 5,100,000, and the hemoglobin content was 14.4 Gm. The weight, which was 31.9 Kg when the patient was admitted to the hospital, had increased to 33 Kg.

On examination one month after the patient was discharged from the hospital, all the cutaneous lesions had disappeared and the eyes were normal. Hyperpigmented spots marked the sites of many of the healed papules. The patient had overcome his aversion to meat and was getting a more adequate diet.

*Comment*—The course of the disease in this patient may be taken as fairly typical of the average instance of vitamin A deficiency with cutaneous and ocular manifestations. There was no clinical evidence of other forms of nutritional deficiency. The slight increase of weight over a period of forty-two days was indicative of the general adequacy of the patient's diet before he entered the hospital. The healing of the cutaneous lesions, which was almost complete after forty-two days, was the most rapid among the patients studied. It seems not unlikely that the halibut liver oil and liver might have been responsible for this difference because of the richer content of vitamin A than was provided other patients in cod liver oil.

Although the keratotic follicular papule was the predominating type of cutaneous lesion, there were two other manifestations of excessive cutaneous keratinization in the form of long and delicate projecting filaments and warty plaques of the knuckles and ankles. We were unable to study these lesions histologically but it was our impression that both the pilosebaceous structures and the openings of the sweat ducts were involved in a common process. In the keratotic plaques it was evident that the epithelium of the entire area was generally hyperkeratotic. The rapidity with which the latter type of lesion healed was a striking demonstration of the effect of therapy. This was the only patient who showed cutaneous changes of the hands and feet.

#### FOLLICULAR DERMATOSIS IN PATIENTS WITHOUT ACROPHALGIA

Because of the occasional long delay in the onset of ocular changes after the appearance of the cutaneous eruption, it is not surprising

that in the course of time patients were seen who presented only the cutaneous signs of disease. Twenty-seven such patients were observed. Of this number, 13 were studied carefully. Nine of the 13 were male and 4 were female, and the ages varied from 16 to 55 years. None showed clinical evidence of alterations in the structure of the conjunctiva and cornea, and only 1 had a history of night blindness. This symptom is frequently the first indication of nutritional ophthalmia and is due to a disturbance in the metabolism of visual purple in the rod cells of the retina.<sup>16</sup>

With one exception all persons concerned were living on a diet inadequate in animal fats and green vegetables, the natural sources of vitamin A or its precursor, carotene. On an average, the diets had been of poor quality for one and a half years before the onset of the eruption. Three patients had lived on a poor and monotonous diet for as long as from three to six years. In the case of the patient whose diet was apparently well balanced and of adequate quantity there was the complicating factor of a first pregnancy, the early and late months of which had been disturbed by severe and persistent nausea and vomiting. This combination of conditions not only increased the nutritional demands of the body but interfered with normal digestion, circumstances which seem sufficient to explain the failure of the diet to provide an adequate amount of vitamin.

There was a wide variation in the duration of the eruption among the 13 patients. In 2 it had been present for eight months; in 1, for six months; and in the others from one to four months. In the group presenting both ocular and cutaneous lesions the eruption appeared from two to four months before the beginning of xerophthalmia. In a comparison of the two groups with respect to the duration of the eruption, it was noted that the patients without sign of ocular involvement had cutaneous lesions for a longer period than those with ocular signs at the time ocular lesions were first observed. This was indicative of an individual variability in the resistance of different tissues to the effect of vitamin A deficiency. It seems reasonable to assume that in some persons xerophthalmia or other abnormalities of the eye may not appear at any time during the course of the deficiency disease. In experimental studies remarkable variation in the manifestations of vitamin A deficiency has been noted. This difference exists both among

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16 Friderici, L. S., and Holm, E. Experimental Contribution to the Study of the Relation Between Night Blindness and Malnutrition. Influence of Deficiency of Fat-Soluble A-Vitamin in the Diet on the Visual Purple in the Eyes of Rats. *Am J Physiol* **73**: 63 (June) 1925. Tansley, K. The Regeneration of Visual Purple. Its Relation to Dark Adaptation and Night Blindness, *J Physiol* **71**: 442 (April) 1931.

species and among members of the same species<sup>17</sup> Xerophthalmia, in any event, is apparently one of the latest manifestations of the disease

The extent of the cutaneous involvement in most of the patients was as great as, and in some greater than, in those persons who also had xerophthalmia or keratomalacia. There was, however, an occasional patient in whom the eruption was confined to a localized area, such as the neck, the buttocks or the arms.

The effect of dietary measures which provided an adequate amount of vitamin A, as well as other food elements, and cod liver oil or vitamin A concentrates was in no respect different from the results of similar treatment in patients having both keratomalacia and the eruption. Nine of the patients were under continuous observation and control for periods of from one to three months, and 1 patient was followed up for six months. The first noticeable sign of improvement was the appearance of moisture on the surface, which not infrequently had been absent, even in the axillary and genito-anal regions. Usually three weeks or more elapsed before exfoliation and extrusion of follicular masses ensued and before diminution in the size of the papules was apparent. In 3 cases there was complete healing of the lesions by the end of the first month, but in the others from two to three months was required before the texture and appearance of the skin approached normal. Occasionally isolated areas of hyperkeratosis persisted for longer periods and as a rule the hyperpigmentation remained beyond the time during which the patients were followed up. Faint scars due to atrophy of tissue usually marked the site of healed follicular lesions. These were clearly visible in 1 patient six months after treatment was commenced.

The following 2 reports of cases are representative of the group in which there were cutaneous lesions without associated xerophthalmia. In addition the patient presented other important physical abnormalities which may have had a direct relationship to vitamin A deficiency.

CASE 3—*History*—A Chinese girl 14 years of age had been a student in an orphanage for six years. She was admitted to the hospital on March 4, 1932, on account of a cutaneous eruption accompanied by lassitude, anorexia and dizziness.

Four or five months before the patient was admitted to the hospital an eruption of small papules appeared on the back of the neck. This itched and disturbed her sleep. Soon afterward similar lesions appeared on both thighs. About one month later papules were seen around the armpits and on the arms.

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17 Wolbach, S. B., and Howe, P. R. Vitamin A Deficiency in the Guinea-Pig. *Arch. Path.* 5:239 (Feb.) 1928. Tilden, E. B., and Miller, E. G., Jr. The Response of the Monkey (*Macacus rhesus*) to Withdrawal of Vitamin A from the Diet. *J. Nutrition* 3:121 (Sept.) 1930. Thatcher, H. S., and Sure, B. Avitaminosis. III. Pathologic Changes in Tissues of the Albino Rat During Early Stages of Vitamin A Deficiency. *Arch. Path.* 13:756 (May) 1932.

and finally on both hips. She noticed that spines projecting from the papules could be removed without pain, but with difficulty, and that their removal left a deep depression. Within a few days the spines were replaced by others.

For several weeks there was no other complaint, but gradually the patient became weak and felt dizzy on sudden motion. Her appetite was impaired. There was no impairment of hearing and no tinnitus. The patient became constipated, the bowels moving once in two or three days. For one month bowel movements had been preceded by some abdominal pain.

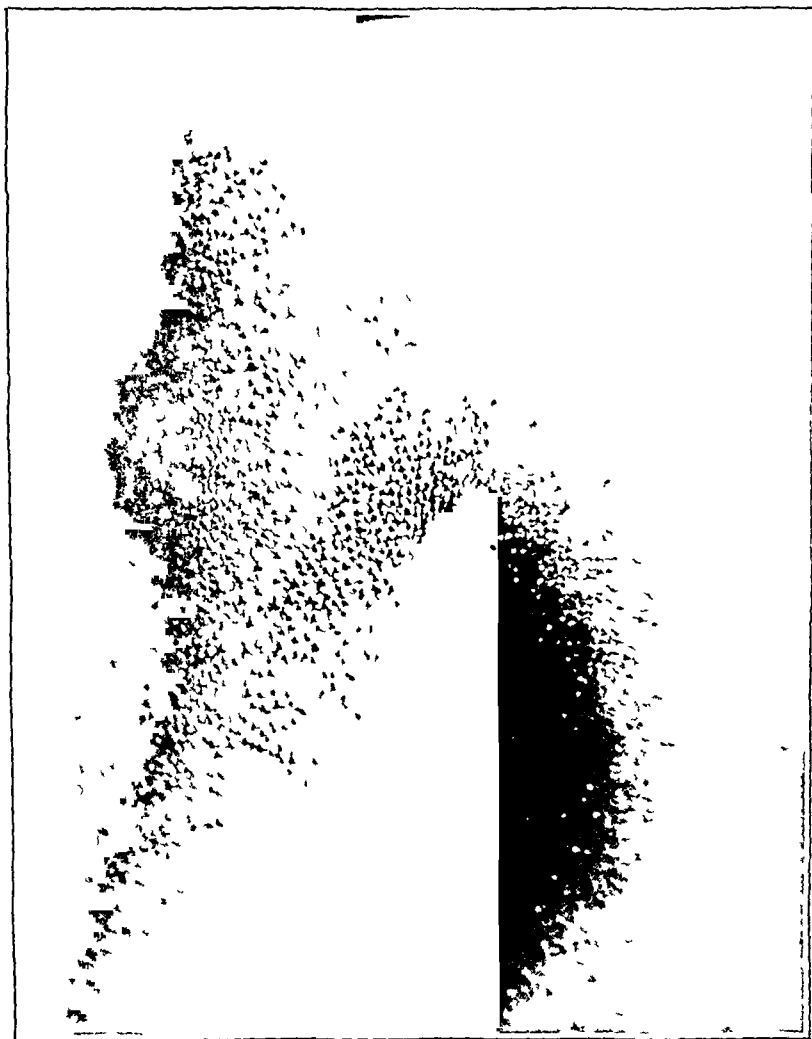


Fig 4 (case 3) —A follicular eruption of five months' duration. The eyes were normal.

*Diet*—Since living in the orphanage, the patient's diet had been insufficient both in variety and in quantity of food. It consisted chiefly of cereals and salted vegetables. Only rarely did the patient have a small amount of meat.

*Physical Examination*—The patient was well developed and looked well nourished. The temperature was 38 C (100.4 F).

The scalp and hair were normal. Distributed over the skin in the areas previously mentioned were pointed papular lesions containing a horny spine which projected from the summit of the papule or in some places appeared as a black-head (fig 4). The fresher lesions were the color of the skin and the older ones

were slightly hyperpigmented. As a whole, the skin was dry and rough. The nails were normal.

The eyes were normal in all respects.

The visible mucous membranes of the nose, mouth and throat were of normal color and texture. The voice was normal.

The lungs were normal on percussion and on auscultation. A systolic murmur was heard at the apex and base of the heart. The blood pressure was normal.

The liver and spleen were not palpable, and the abdomen was soft. Tenderness was not present.

The tendon reflexes were low.

*Laboratory Examinations*—The urine contained many epithelial cells. There were 4,900,000 erythrocytes per cubic millimeter of blood, with a hemoglobin content of 94 per cent, and 5,100 leukocytes, of which 56.5 per cent were neutrophils, 5.5 per cent eosinophils and 42 per cent lymphocytes. The reticulocyte count was 0.6 per cent.

The Wassermann and Kahn reactions of the blood were negative.

The stools contained ova of *Ascaris*.

*Course and Treatment*—A well balanced diet was given. The stools on several occasions contained undigested food. *Ascaris* worms were passed after treatment. Ten days after the patient was admitted to the hospital about a third of the cutaneous spines had disappeared. Local treatment was not given. At this time 100 Gm of liver was added to the diet twice a day. Dizziness and lassitude, prominent symptoms when the patient was admitted to the hospital, soon disappeared. After one month in the hospital the patient was discharged. The condition of the skin was much improved. By arrangement with the orphanage, where the patient was living, a small amount of liver was provided as a supplementary diet. Otherwise, she continued to receive the same kind of food as she had before the appearance of the cutaneous eruption. Three months later the patient had a normal skin.

*Comment*—The cutaneous eruption in this case was less extensive than usual but in other respects it conformed to the type generally observed. The distribution of the lesions was that of the early stage of the dermatosis. When the eruption does not progress beyond a localized group of papules, one or more of the areas involved in this case is the customary site of involvement.

On an ordinary hospital diet and liver the cutaneous lesions healed rapidly. The addition of a small amount of liver to the customary diet of the patient while she was living in the orphanage apparently provided an adequate amount of vitamin A.

Lassitude and dizziness were the only subjective complaints. These symptoms soon disappeared after the patient was given an adequate diet. The cause of vertigo which was noticed only when the position of the head was suddenly changed, may have been related to some pathologic change in the vestibular apparatus incident to vitamin deficiency. In 1 other patient bilateral deafness developed simultaneously with the onset of keratomalacia and without any evidence of otitis media or disease of the external ear.

The presence of many epithelial cells in the urine may be taken as indicative of involvement of the urinary tract by the disease. In 1883 Leber<sup>18</sup> described the occurrence of desquamation of renal epithelium in a patient who died with keratomalacia. More recently Herbert<sup>19</sup> reported that large quantities of desquamated epithelium were noted in severe cases of avitaminosis A. Blackfan and Wolbach<sup>2</sup> pointed out that the second most common site for the appearance of keratinizing metaplasia in infants suffering from vitamin A deficiency is the pelvis of the kidney. Among the 31 patients comprising the two groups discussed in this paper, only 3 showed an abnormally large number of epithelial cells in the urine.

**CASE 4—History**—A Chinese student 19 years of age was admitted to the hospital on Feb. 16, 1934, with a diagnosis of chronic dysentery.

At intervals for one year the patient had had from five to six bowel movements daily, the stools frequently containing blood and pus. Just prior to his admission to the hospital the condition had become more acute. Six months previously he noticed blurring of vision at night, and at about the same time an eruption appeared, which was still present.

**Diet**—Cereals, cabbage and bean curd were the principal components of the diet. The patient seldom had meat, fish or eggs.

**Physical Examination**—The patient was slightly undernourished and pale. There was some discomfort from abdominal pain.

Over the extensor surface of both the lower and the upper extremities the hair follicles were elevated and hyperkeratotic. A long spine projected from many of them. The hair was normal. The nails were pale but not deformed. Pigmentation was increased over the dorsum of both hands, and the skin over the knuckles was somewhat thickened and rough. The lips were dry, pale and slightly fissured. Fissures were present at the angles of the mouth. The visible mucous membranes were normal. There was tenderness over both maxillary sinuses.

The superficial lymph nodes were generally palpable, firm and discrete.

Except for papillary trachoma, the eyes were normal.

There was slight impairment of resonance over the upper lobe of the right lung anteriorly and posteriorly. The breath sounds were normal. The heart was normal.

The abdomen was tender, especially in the lower portion. The reflexes were normal. The temperature was 38.5 C (101.3 F).

**Laboratory Examination**—The urine was normal. There was secondary anemia, the erythrocyte count being 2,080,000 per cubic millimeter, with 8.9 Gm of hemoglobin per hundred cubic centimeters. There were 6,400 leukocytes per cubic millimeter, of which 55 per cent were polymorphonuclear neutrophils and 39 per cent lymphocytes. The reticulocyte count was 0.5 per cent. The platelets numbered 311,000 per cubic millimeter. There were slight anisocytosis and poikilocytosis.

18 Leber T. Die Xerosis der Conjunctiva und Cornea kleiner Kinder, Arch Ophth. 29:328, 1883.

19 Herbert H. Discussion Tr. Ophth. Soc. U. Kingdom 50:235, 1931.



The nonprotein nitrogen content of the blood was 21 mg per hundred cubic centimeters, the albumin content, 292 per cent, and the globulin content, 356 per cent

Cultures of stools showed *Bacillus dysenteriae* of the Shiga type

The Wassermann and Kahn reactions of the blood were negative

*Course and Treatment*—The patient was given a soft diet and was treated for bacillary dysentery. A sigmoidoscopy showed the colon to be congested and edematous, with a few very small ulcers and scars. After nine days in the hospital the stools were normal in character and frequency. During the remainder of his stay in the hospital, the patient received a full diet and 30 cc of cod liver oil daily. By the fourteenth day of treatment the cutaneous lesions had commenced to disappear. When he left the hospital fifty-five days after he was admitted, a few follicular papules remained, the bowel movements were normal and the stools did not contain pathogenic organisms. The blood picture was normal, and the body weight had increased 4.2 Kg.

*Comment*—Although the patient was subsisting on a poor diet, no signs of nutritional deficiency appeared until after the development of chronic bacillary dysentery. Serious dysfunction of the gastrointestinal tract or infectious processes which interfere with normal digestion and assimilation of food have been observed to give rise to certain of the vitamin deficiencies in particular to pellagra.<sup>20</sup> The probability of such occurrences is increased under conditions of dietary inadequacy such as existed in the case of the patient just described.

After the disappearance of the dysentery, the hyperkeratotic condition of the skin and hair follicles responded to dietary and cod liver oil therapy in a fairly prompt and satisfactory manner. However after forty-five days of treatment isolated areas of modified keratotic papules remained. The texture of the skin did not regain normal smoothness until after three months and hyperpigmentation of the scars persisted longer.

#### HISTOPATHOLOGIC PICTURE

Minute examination of specimens of skin taken from patients in both groups of cases revealed that the pathologic process was primarily hyperkeratinization of the lining epithelium of the hair follicles. Significant differences in histologic detail did not exist between specimens from individual patients of the same group or from the two groups. Such differences as did exist were those related to the stage of development of the eruptive lesion or to the normal variation in anatomic structure.

The hair follicles were obstructed and frequently greatly distended particularly at the upper portion, by a dense mass of lamellated cornified

20 Ellis, R. W. B. Pellagra Secondary to Gastro-Intestinal Disease, *Am J Dis Child* **39** 1036 (May) 1930. Lusterman, G. B., and O'Leary, P. A. Pellagra Secondary to Benign and Carcinomatous Lesions and Dysfunction of the Gastro-Intestinal Tract. Report of Thirteen Cases. *Arch Int Med* **47** 633 (April) 1931.

cells, with and without nuclei. Coiled atrophic hairs were found in some of the horny masses. Hyperplasia of the epidermal cells adjacent to the hair follicles occurred in the papulated areas, where there was also an increased intracellular pigmentation. Moderate hyperkeratinization of the surface epithelium extended beyond the papules. Epithelial proliferation likewise was noted at the sides of some of the hair follicles.



Fig 5—Hyperkeratosis of a hair follicle, showing atrophy of the papillary part, with associated epithelial hyperplasia

below the point of obstruction. The keratinizing epithelium of the dilated follicle was granular to a considerable extent. The papillary part of the follicle was atrophic and in places was completely separated from the body of the follicle. In 1 case it was occasionally cystic and filled with desquamated keratinized cells.

There was absence of sebaceous glands in connection with the damaged follicles and the site of the gland was occupied by a moderate infiltration of mononuclear lymphoid cells. This cellular infiltration

also extended to the immediate perifollicular tissues, where the blood capillaries were numerous. Hemorrhage was not present around the follicles or elsewhere in the skin.

The structure of the sweat glands and their related ducts was involved in much the same way as the pilosebaceous elements, although not to an extent sufficient to produce a clinically recognizable lesion. The upper



Fig 6—Formation of a cyst in the region of a hyperkeratotic hair follicle. The cyst contains desquamated cornified cells.

part of the sweat ducts, or that portion lying within the epidermis, was occluded to varying depths by desquamated cornified cells. The epithelial cells surrounding the ducts contained keratohyaline granules. In places the cornified material extended as a tapering wedge into the deeper segment of the duct. Bands of stratified epithelium accompanied some of the ducts into the corium. The normal structure of the duct

in this location consists of a double row of cuboidal epithelial cells and a delicate hyaline inner membrane. Degeneration of the coil glands although not frequent, was detectable as a flattening and an irregularity of the secretory cells. No evidence of the formation of a cyst as a result of occlusion of the duct was observed.

Pustulation of the skin, which was infrequent, developed in the follicular papules. The earliest sign of this process was the appearance of leukocytes among the keratinized cells adjacent to the epithelium of

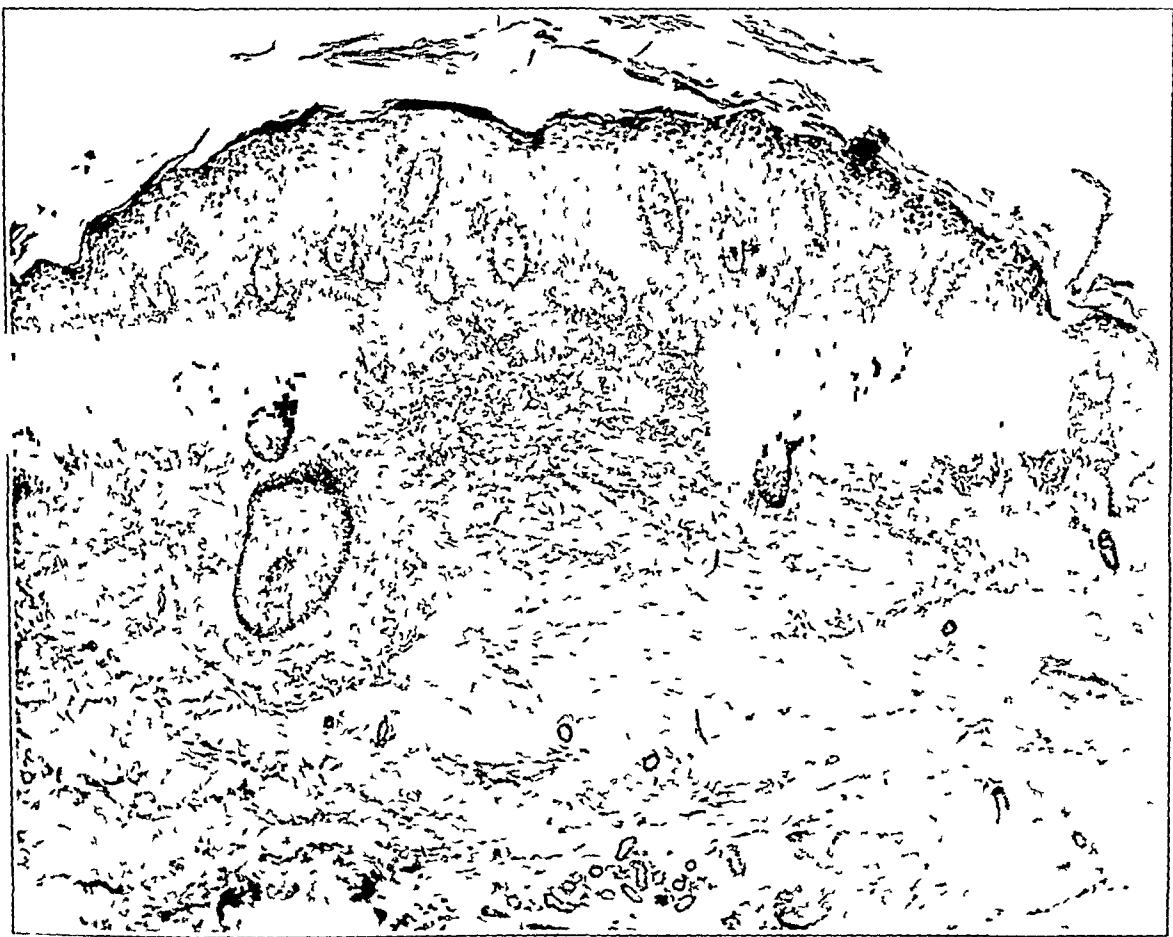


Fig 7—Epithelial hyperplasia of the epidermis in the region of a hair follicle

the distended follicle. Ulceration began in this disintegration of the follicular wall with subsequent involvement of the perifollicular tissues.

The atrophy and epithelial metaplasia occurring in the pilosebaceous and sweat gland structures were comparable to those changes described in other epithelial structures as the effect of vitamin A deficiency and constituted important evidence of the specific nature of the cutaneous lesions.

Whether hyperkeratinization of the involved structures preceded the degenerative changes in the glands of the skin particularly in the sebaceous glands or whether the reverse occurred is not known. It

can be stated only that in the sections examined the fat glands had disappeared from the follicles which were keratotic. That the function of the sweat glands was almost entirely suppressed in many of the patients seemed certain. The failure of function was apparently not entirely dependent on occlusion of the ducts. There was absence of sweating in regions where there was very little hyperkeratosis of the surface epithelium, and a return of surface moisture was detected soon after treatment commenced and before any appreciable decrease in keratinization of the skin was observed.

#### DISTRIBUTION OF CUTANEOUS LESIONS ACCORDING TO AGE

Impressed by the frequency with which the eruption appears in young adults and by the fact that in the reports on xerophthalmia in infants and children no reference has been made to similar abnormalities of the skin other than general xerosis, a study of the distribution of the dermatosis according to age was undertaken. The clinical records of all patients showing typical xerophthalmia or keratomalacia admitted to the hospital of the Peiping Union Medical College were reviewed. Included also were those of the patients previously considered, who had only follicular dermatosis. The results of this study showed that the age of the patient is an important factor in determining the involvement of the skin.

A total of 207 persons were examined in whom the condition fulfilled the requirements for selection. Of this number 180 presented typical ocular manifestations of the deficiency disease, and 27 only the cutaneous eruption.

It was soon apparent that most of the patients with the dermatosis were over 15 years of age. On this basis the patients were divided into four groups according to age, each of which covered a span of fifteen years. The results of this division are presented in the table.

It is evident that adults were as often the victims of xerophthalmia as were infants and children. The youngest patient was 1½ months old, and the oldest was 57 years of age. The highest incidence of xerophthalmia in the series occurred during the first year of life. Thirty-nine patients were under 1 year of age, and 76 were 5 years of age or under.

Sex.—There was an impressive difference in the distribution of the disease according to sex between patients from 1 to 15 years of age and those from 16 to 30 years. For the first fifteen years of life males and females were about equally affected, but during the second fifteen year period almost the entire group was composed of males. Not a single case of vitamin A deficiency in a woman appeared after the age of 30 years. The preponderance in men is explained in part at least by the nature of their occupations. Many men were soldiers or

apprentices, whose diets as a rule are poor in quality. Whether the factor of sex itself enters into the difference in susceptibility between sexes is an open question, but there is some reason to think that it does.

*Incidence of Follicular Keratosis in Patients with Xerophthalmia*—Among 87 patients with xerophthalmia between the ages of 1 month and 15 years, 2 had follicular keratosis of the skin. Among 80 patients with xerophthalmia between the ages of 16 and 30 years, 24 had the eruption. In other words, about 2 per cent of those under 15 years and 30 per cent of those over this age were subject to the dermatosis. It is also of interest that the eruption occurred in only two among 13 patients between the ages of 31 and 57 years. The incidence of simple xerosis of the skin, or xeroderma, in the first group was about 30 per cent and in the second, 15 per cent. If the patients showing the

*Distribution of Ocular and Cutaneous Lesions According to Age in Two Hundred and Seven Patients with Avitaminosis A*

Group	Age	Number of Patients	Sex		Xerophthalmia		Follicular keratosis		Xeroderma*		Pvoderma	
			Male	Female	No	Per Cent	No	Per Cent	No	Per Cent	No	Per Cent
1	2 mo. to 15 yr.	91	49	42	87	95.5	6	6.6	26	28.6	7	7.7
2	16 to 30 yr.	103	94	9	80	77.6	47	45.6	12	11.6	8	7.8
3	31 to 45 yr.	8	8	0	8	100.0	1	12.5	1	12.5	2	25.0
4	46 to 60 yr.	5	5	0	5	100.0	1	20.0	0	0.0	1	20.0
Total		207	156	51	180	86.9	55	26.6	39	18.8	18	8.7

\* Patients with follicular keratosis were not included.

follicular dermatosis but no ocular lesions are included in the summary, a significant difference is not made in the general distribution of the dermatosis according to age.

It can be seen from these figures that the cutaneous eruption was a characteristic of vitamin A deficiency only after the patient had attained sexual maturity. Before the age of puberty the only common abnormality of the skin was general xerosis. The follicular eruption has not been seen in an infant and only 2 children with xerophthalmia, 4 and 5 years old, respectively, showed any indication of it. In these 2 patients there was a distinct prominence of the hair follicles, owing to the presence of intrafollicular hyperkeratosis, but papulation as the result of appreciable perifollicular infiltration was not developed to the degree usual in older persons. Neither were the keratotic follicles as numerous or as widely distributed. Four children in the first age group who presented only the follicular eruption were from 14 to 15 years old, of an age so near that of the second group that they may be considered as members of it with respect to their sexual development.

*Incidence of Xeroderma*—It is remarkable that the incidence of simple xerosis among infants and children with xerophthalmia equaled

that of follicular keratosis among adults similarly affected. It seems probable that simple xerosis of the skin bears more than a coincidental relationship to the avitaminosis, although there is as yet no histologic proof to support this opinion. Additional evidence of this relationship is found in the occurrence of the same condition in adults who do not show any sign of dehydration or general malnutrition. In such cases excessive dryness of the skin is a phenomenon which may appear independent of the follicular keratosis or as a prodromal sign of the development of the eruption. In either event the xerotic condition responds to dietary therapy in much the same way as the follicular keratosis.

*Relation to Sexual Development*—In attempting to explain the difference between the cutaneous reaction in children and that in adults, it is necessary to consider the developmental changes in the skin incidental to age. The principal differences in the reaction in this respect are related to the pilosebaceous structures. From birth onward these structures gradually undergo a process of development both in form and in function. The character of the changes in the hair, and the activity of the sebaceous glands are considerably modified by age. It is only after the fourth or fifth year of life that sebaceous secretion is well established. At the age of puberty and through adolescence the secretory function of these glands reaches a maximum. With senescence the reverse process ensues. These normal variations apparently condition the response of the structures to disease. Examples of this are found in the mycotic infections of the scalp peculiar to childhood and in such conditions as acne developing during the period of adolescence. It is perhaps of some significance, therefore, that the youngest patients in whom follicular keratosis occurred were 4 and 5 years of age and that only 2 patients over 30 years old with xerophthalmia had the eruption while a third of those of adolescent age were affected.

#### OTHER CUTANEOUS ABNORMALITIES

*Pyoderma*—Bloch<sup>21</sup> and Spence,<sup>22</sup> among others, called attention to the high incidence of infection of the skin among infants and children afflicted with xerophthalmia or keratomalacia. They attributed an increased susceptibility to pyogenic infection to a deficiency of vitamin A in these patients. Mackay<sup>23</sup> published an extensive review in which

21 Bloch, C. E. Effects of Deficiency in Vitamins in Infancy. Caries of the Teeth and Vitamins, *Am J Dis Child* **42** 263 (Aug) 1931.

22 Spence, J. C. A Clinical Study of Nutritional Xerophthalmia and Night Blindness, *Arch Dis Childhood* **6** 17, 1931.

23 Mackay, H. M. M. Vitamin A Deficiency in Children. I. Present Knowledge of the Clinical Effects of Vitamin A Deficiency, with Special Reference to Children. *Arch Dis Childhood* **9** 65, 1934. II. Vitamin A Requirements of Babies. Skin Lesions and Vitamin A Deficiency, *ibid* **9** 133, 1934.

emphasis was placed on this aspect of the disease. According to her, the earliest clinical evidence of vitamin A deficiency is an increased susceptibility of the skin to "boils, sores, impetigo, napkin rash or other evidence of skin sepsis."

Among the patients observed in Peiping, infections of the skin, such as furunculosis, impetigo, abscesses and other more minor diseases attributable to pyogenic bacteria, were not of frequent occurrence. Less than 10 per cent of all patients (table) had signs of pyogenic dermatitis. Mycotic infections of the scalp, which are common among children in this locality, occurred infrequently.

Of the 15 patients with keratomalacia associated with the follicular keratosis whose cases we reported in 1930, a third had pustular lesions of the skin, usually on the extremities, which led to the formation of ecthymatous ulcers. As a rule there were not over four or five ulcers, although in 1 patient they were numerous and closely resembled secondary ulcerative syphilids. This was in the patient whose case was described by Pillat as one of dermomalacia. Occurrences such as this are exceptional, only 1 similar case having been observed since that time. Scabies was a complicating infection in 4 of the 15 patients. Among the 31 patients whose cases were reviewed in the first part of this paper, 4 had a pyogenic cutaneous infection, 3 had fungous infections of the scalp, and 1 had scabies.

*Comedones*—Comedones of the face were one of the conspicuous cutaneous abnormalities. They were more numerous and keratotic than is usual in simple acne. Only rarely did pustules form around the comedones. The acne-like condition was present not only in adolescent patients but in older persons as well and as a rule disappeared with the general improvement of the patient. Instances occurred in which the comedones were the only evidence of follicular involvement. The condition was not observed among infants and children under 15 years of age, but it was present in about 11 per cent of all patients between 16 and 30 years of age who did not have a follicular eruption of the trunk and extremities. Other than general xerosis, comedones were the only cutaneous abnormality presented by these patients.

#### SPECIFICITY OF THE DERMATOSIS

In determining the relationship of the dermatosis to vitamin A deficiency it is necessary to consider other nutritional deficiencies as possible factors in the causation of the cutaneous changes. It is well recognized that in human patients a diet deficient in one vitamin is frequently deficient in others. For this reason a single patient may show clinical evidence of more than one deficiency disease, making it necessary to identify each sign and symptom with respect to the



particular dietary component responsible for its presence. When the classic signs of more than one type of avitaminosis occur in a patient this may not be difficult, but in the event that the clinical picture is complicated by the presence of anatomic or functional abnormalities previously unrelated to the disease the etiologic identification of such manifestations offers a much greater problem. This is particularly true if the familiar signs of the deficiency disease happen to be absent.

In this connection we previously called attention to the fact that follicular keratosis similar to that occurring in vitamin A deficiency, was observed in cases of scurvy by Nicolau,<sup>24</sup> Wiltshire,<sup>25</sup> Theodorescou<sup>26</sup> and others. The eruption differed in only one essential. With scurvy, hemorrhage was present in the region of the hyperkeratotic follicles. Otherwise, the histologic changes, which were carefully described by Nicolau, did not present significant variations from those seen in the patients we have studied and bear no relation to the pathologic changes of scurvy. The possibility of multiple dietary deficiencies was not considered by the aforementioned observers, although some of the patients were known to have had night blindness.

Among the cases reported by Nicolau, the eruption appeared in some patients who showed no signs of scurvy, and in others it preceded the onset of scorbutic lesions. In the 4 cases reported in detail, there was a history of night blindness in 1, but in none was there reference to any other ocular abnormality. Theodorescu, who was familiar with the observations of Nicolau, described a case in which the eruption had been present for three months and was associated with a progressive diminution of visual acuity after dark. Later, signs of scurvy developed. It was the opinion of Theodorescu that the eruption "constitutes an early symptom of the disease (scurvy) preceding night blindness, general asthenia and neuralgia." In recent years, experimental and clinical studies<sup>27</sup> have shown that night blindness caused by faulty nutrition is the result of a deficiency in vitamin A.

Scheer and Keil<sup>23</sup> called attention to the possibility of vitamin C being the responsible factor in the production of follicular lesions. They were unable to accept an explanation of the cutaneous eruption on the

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24 Nicolau, S. Étude sur une eruption folliculaire et perifolliculaire dans le scorbut. Dermatite papulokeratosique scorbutique, *Ann de dermat et syph* **7** 399, 1918-1919.

25 Wiltshire, H. Hyperkeratosis of the Hair Follicles in Scurvy, *Lancet* **2** 564 (Sept 27) 1919.

26 Theodorescou, S. Sur un cas de dermatite papulokeratosique scorbutique, *Ann de dermat et syph* **9** 581, 1928.

27 Holme, E. Demonstration of Hemeralopia in Rats Nourished on Food Devoid of Fat-Soluble-A-Vitamin, *Am J Physiol* **73** 79 (June) 1925. Askroyd W. R. Night Blindness Due to Vitamin Deficiency, *Tr Ophth Soc U Kingdom* **50** 230, 1930. Spence<sup>22</sup>

basis of a dual pathologic process depending on a coincidental lack of vitamins A and C. In support of this opinion they cited 2 cases in which the usual manifestations of scurvy were accompanied by follicular keratosis. Other than the presence of hemorrhage in the perifollicular tissues in 1 of the cases reported, there was no essential difference between the cutaneous lesions described and those occurring in cases of frank vitamin A deficiency.

No critical therapeutic test has yet been undertaken in connection with scurvy and the follicular dermatosis comparable to that carried out by Loewenthal in cases of the eruption and xerophthalmia. If one bears in mind the present conception of the pathologic characteristics of the two deficiency diseases, it seems reasonable to assume that the epithelial changes occasionally found in association with scurvy are related to a lack of vitamin A rather than to a lack of vitamin C. This is equally true of other types of avitaminosis, such as pellagra,<sup>28</sup> in which similar lesions of the skin have been observed.

Clinical evidence of multiple dietary deficiencies was present in a number of the 180 patients with typical xerophthalmia whose cases we reviewed. Twenty-four had signs of rickets. There was 1 patient with scurvy. Nutritional edema, although caused by a deficiency of protein rather than by a lack of a vitamin, occurred in 8 patients. Follicular keratosis was not noted in association with rickets in any case. Xerophthalmia was the only manifestation of vitamin A deficiency in the patient who had scurvy. Six patients with nutritional edema had xerophthalmia, and 2 had xerophthalmia and follicular keratosis.

During the same period in which the cases of vitamin A deficiency were observed, 257 cases of rickets, 88 cases of beriberi, 10 cases of pellagra and 11 cases of scurvy were observed in the hospital. With 4 exceptions, the only instances of follicular keratosis in these cases were those already mentioned. The exceptions included 1 case each of beriberi and pellagra and 2 cases of nutritional edema.

It is apparent, on the basis of this experience, that the development of follicular keratosis of the skin is common only to those persons showing the classic signs of vitamin A deficiency. This fact and the evidence previously presented leave little doubt as to the direct relationship of the dermatosis to a deficiency of vitamin A.

#### SUMMARY

Further clinical observations tend to confirm the specific nature of the hyperkeratosis of hair follicles which frequently occurs in association with xerophthalmia in young adults. Observations on cases of the

<sup>28</sup> Stannus, H. S. Pellagra in Niasaland, *Tr. Soc. Trop. Med. & Hyg.* 5:112, 1911-1912.

dermatosis in which the classic ocular signs of vitamin A deficiency were absent indicated that the skin may present the only clinically detectable manifestation of this deficiency disease. The therapeutic response of the cutaneous disease in such cases corresponded to that observed in cases in which there are ocular changes.

The histologic characteristics of the dermatosis are analogous to those occurring in other epithelial structures of the body as a result of vitamin A deficiency.

Abeyance of the secretory function of the skin was a conspicuous phenomenon.

Among 207 persons with vitamin A deficiency from 2 months to 57 years of age, the follicular eruption was characteristic of the disease in those who had attained sexual maturity. The eruption rarely occurred before this age and was not observed among infants. There is evidence that in infancy and childhood vitamin A deficiency may be responsible for simple xerosis of the skin, which may also be present in adults, frequently preceding the onset of follicular keratosis.

Pyogenic cutaneous involvement was not a prominent feature of the disease.

# LYMPHOGRANULOMA INGUINALE

## II THE CULTIVATION OF THE VIRUS IN MICE AND ITS USE IN THE PREPARATION OF FRIE ANTIGEN

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The object of this work was to culture in the brains of mice a virus of lymphogranuloma inguinale. The work was undertaken, first, to study the properties of the virus and, second, to make use of such a virus for the preparation of Frie antigen.

The first investigators to discover that the virus of lymphogranuloma inguinale is transmissible to mice via the intracerebral route were Levaditi, Ravaut and Schoen<sup>1</sup>. They employed an emulsion of lymphogranulomatous monkey brain as the original inoculum. They concluded, however, that the mouse is not constantly susceptible to the virus of lymphogranuloma inguinale as not all the animals inoculated with the same material and by the same route showed signs of the disease.

The following year Findlay<sup>2</sup> transmitted eleven strains of virus to mice, the primary inoculum being either human lymphogranulomatous material or monkey brain. He found that strains of the virus varied in the ease with which they were transmitted, certain strains tending to die after a single passage and only one being capable of transmission for as many as eleven passages. The average period elapsing between inoculation and death was thirty-four days, with a maximum of ninety-four and a minimum of five days. The virus did not become fixed for the brains of mice.

E. Wassen,<sup>3</sup> on the other hand, was able to pass the virus in the brains of mice through twelve passages and he found that the virulence

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1 Levaditi C, Ravaut P, and Schoen, R. Receptivité de la souris à l'égard du virus de la maladie de Nicolas et Favre, *Compt rend Soc de biol* **109** 285, 1932.

2 Findlay G M. Experiments on the Transmission of the Virus of Climatic Bubo (Lymphogranuloma Inguinale) to Animals. *Tr Roy Soc Trop Med & Hyg* **27** 35 (June) 1933.

3 Wassen F. Receptivité de la souris blanche à l'égard du virus lymphogranulomateux (maladie de Nicolas et Favre). *Compt rend Soc de biol* **114** 493, 1933.

increased with successive passages, so that toward the last passage from 50 to 60 per cent of the animals died in from three to six days and 100 per cent showed meningo-encephalitis. He was also able to prepare from material from the mice used for the first four successive passages Frei antigens which gave reactions as strong as those produced by antigens prepared from pus from human beings.

In a subsequent communication Levaditi and his co-workers<sup>4</sup> corroborated Wassen's findings. They observed that lesions of the motor system of mice appeared more frequently in the animals used for the later passages than in those employed for the earlier ones. They carried the virus through sixteen passages in all and regarded the process as one of adaptation of the virus to mice.

#### SOURCE OF THE VIRUS

Material for this study was obtained originally from a patient who had the inguinal type of lymphogranuloma inguinale. The clinical history of the patient follows:

A M. was a Negro aged 34. On Feb. 10, 1934, one month after sexual intercourse, hard, tender swellings arose in each groin unaccompanied by any noticeable penile lesion or urethral discharge. The swellings attained a maximum size in two weeks and had not diminished in size when the patient was admitted to the second surgical division (Cornell) of the Bellevue Hospital, on April 6. At that time each groin presented a firm, slightly tender, somewhat fluctuant, fixed, nodular mass, approximately the size of half an orange. The overlying skin was unbroken, brawny and reddened. There was an abrasive lesion 2 cm. in diameter on the long, uncircumcised prepuce. This lesion had appeared on March 26. Both the masses in the groins were aspirated and yielded 3 cc. of thick, inodorous pus, which showed no organisms in a direct smear and was bacteriologically sterile on aerobic and anaerobic culture. The pus was divided into three parts. One part was used to make a Frei antigen; another part was dried from the frozen state, and the remainder was reserved for intracerebral inoculation into mice.

A positive Frei reaction was given by the patient when heterologous antigen was used, and the Frei antigen made from his pus elicited a strong reaction on intradermal inoculation into another lymphogranulomatous person but did not produce any reaction in a normal subject.

The Ito-Reenstierna reaction and the Wassermann reaction were negative.

The masses in the groins were excised on the day following aspiration. They consisted of matted glands, fat and thickened periglandular tissue. The glands were separated from the surrounding tissue and showed on section a collection of small purulent foci, which were visible macroscopically. The glandular material

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<sup>4</sup> Levaditi, C., Ravaut, P., Schoen, R., and Levaditi, I. *Entretien du virus lymphogranulomateux (maladie de Nicolas et Favre)*, *Compt. rend. Soc. de biol.* **114**: 499, 1933.

was divided into two parts, of which one was dried from the frozen state and the other was set aside for intracerebral inoculation into mice

#### MATERIAL AND METHODS

The pus and the glandular material obtained from the patient were both used for the primary intracerebral inoculation of mice and were labeled material 27 and material 28, respectively. Animals inoculated with pus were kept separate from those inoculated with glandular material, and each series of mice received one type of material only. The object of this was twofold. First, the results obtained with one material were regarded as a check on those obtained with the other, and, second, the double series reduced the risk of losing the strain of virus. The inoculum used for all passages except the first and the second consisted of an emulsion of the brain of a mouse dead or dying as the result of a previous intracerebral inoculation with lymphogranulomatous mouse brain. The first inoculum consisted of material 27 or 28, and the second consisted of a suspension of the brain of a mouse dead or dying as a result of the previous inoculation with the material from the human subject.

The material to be used for inoculation was finely emulsified in a sterile mortar with a diluent as soon as possible after collection, 1 part of material being used to from 25 to 55 parts of diluent. Sterile sand was added in the case of the glandular material and was removed by centrifugation. The diluents used were a sterile buffered physiologic solution of sodium chloride of  $pH$  7.1, a sterile unbuffered, physiologic solution of sodium chloride, broth of  $pH$  8, ascitic fluid, Tyrode's solution and sterile distilled water. The primary inoculums of pus and glandular material were emulsified in distilled water, as were also the inoculums used for the five succeeding passages in mice. In the next twenty-five passages in mice the material used for inoculation was suspended in a sterile buffered physiologic solution of sodium chloride. This solution was composed of sodium chloride 5 parts, di-sodium hydrogen phosphate ( $Na_2HPO_4 \cdot 12 H_2O$ ) 1.431 parts, anhydrous potassium di-hydrogen phosphate ( $KH_2PO_4$ ) 0.363 part and phenol crystals 4 parts, dissolved in 1 liter of distilled water and sterilized in the autoclave. The amount of phenol used had no apparent effect on the virus. The mice used for the thirty-first and succeeding passages received material emulsified in all the diluents mentioned, with the exception of sterile distilled water.

A portion of the inoculum was cultured aerobically and anaerobically at the time of inoculation, and all mice which had received material that yielded a bacterial growth after forty-eight hours were discarded.

Frei antigen was prepared from lymphogranulomatous mouse brains by emulsifying them in a sterile mortar with a sterile buffered physiologic solution of sodium chloride of  $pH$  7.1 or with an unbuffered sterile physiologic solution of sodium chloride. The dilutions varied between 1:25 and 1:10, and the emulsions were heated according to the method of Frei.

White mice weighing from 15 to 20 Gm were used for the greater part of this work. In the earlier passages piebald mice were occasionally employed. Inoculations were made with the animal under ether anesthesia. With a 26 gauge needle and a 0.25 cc syringe the material was introduced through the left parietal bone into the underlying cerebrum. The volume of emulsion used for inoculation was 0.03 cc.

Brains from mice used in each passage of the virus were also taken for histologic study. They were fixed in a dilute solution of formaldehyde U. S. P. (1:10) made neutral and paraffin sections were made from them. The sections

were stained with Delafield's hematoxylin and an aqueous solution of eosin MacCallum's modification of the Goodpasture stain for micro-organisms and Loyez's myelin stain<sup>6</sup>

#### THE BEHAVIOR OF MICE AFTER INTRACEREBRAL INOCULATION WITH THE VIRUS OF LYMPHOGRANULOMA INGUINALE

Signs of illness appeared on the day following inoculation. The animals first showed reduced activity, roughening of the coats and anorexia. The apathy soon deepened and was accompanied by humping of the back, gumming of the eyes and considerable emaciation. Many of the mice at this stage showed coarse tremors involving the whole body. Shortly before death spastic paralysis of the hind limbs usually developed, and priapism was often a terminal sign. A few animals displayed hyperirritability and showed an exaggerated response to slight tactile stimuli, others exhibited clonic contractions, during which they rotated about a horizontal axis.

Although 100 per cent of the animals became sick, not all of the mice used for each passage died. A certain proportion, depending on the concentration of the material used for inoculation, recovered after being desperately ill, and only a few apparent relapses occurred after an animal began to improve.

#### RESULTS

*Passage in Mice*—As the results obtained with material 27 so closely agreed in every respect with those obtained with material 28, it was decided to combine the data relating to the two materials, the figures given in this section, therefore, as well as those used in the preparation of the chart (fig. 1) represent the true average results obtained with each passage of the two materials.

The animals which received the primary inoculum of a 20 per cent suspension of pus or glandular material from the human subject survived, on an average eleven and eight-tenths days. The next eleven passages in mice were made with a 40 per cent suspension of the brain of an animal dying as a result of a previous inoculation. Beginning with the first passage, there was a gradual but well marked diminution in the period elapsing between inoculation and death until the eleventh passage was reached. Similarly, there was a definite increase in the mortality rate of inoculated animals. The shortening of the period between inoculation and death involved such frequent passages that the strength of the inoculum was reduced to 20 per cent for passages twelve to twenty-one, inclusive. The effect of this reduction in strength was to make the average time between inoculation and death longer. Thus, whereas for the first eleven passages the average length of this period was five and three-tenths days, with a maximum and a minimum of thirty and two days, respectively, for the twelfth to the twenty-first passage it was seven days, with a maximum and a minimum of fifty-eight and two days. Similarly, the mortality rate began to fall concurrently with the use of the weaker inoculum. The time elapsing between inoculation and death and the mortality rate were not quite as uniform when the lower concentration of

5 McClung, C. E. Handbook of Microscopical Technique, New York, Paul B. Hoeber, Inc., 1929, p. 105.

6 This is a modification of the Weigert iron hematoxylin stain.

inoculum was used as when the high concentration was employed. Whether this phenomenon was inherent in the virus is difficult to conclude, as during a greater part of the passages between the twelfth and the twenty-first there was a temporary change of assistants. In the twenty-first passage less than 23 per cent of the inoculated animals died. Hence, beginning with the twenty-second passage the strength of the inoculum was increased in order to prevent the virus from dying out completely. As a consequence, the length of the period elapsing between inoculation and death fell in six passages to a point lower than any previously reached, and the mortality in the same interval reached 100 per cent. The death of all the animals used for the twenty-seventh and twenty-eighth passages in as

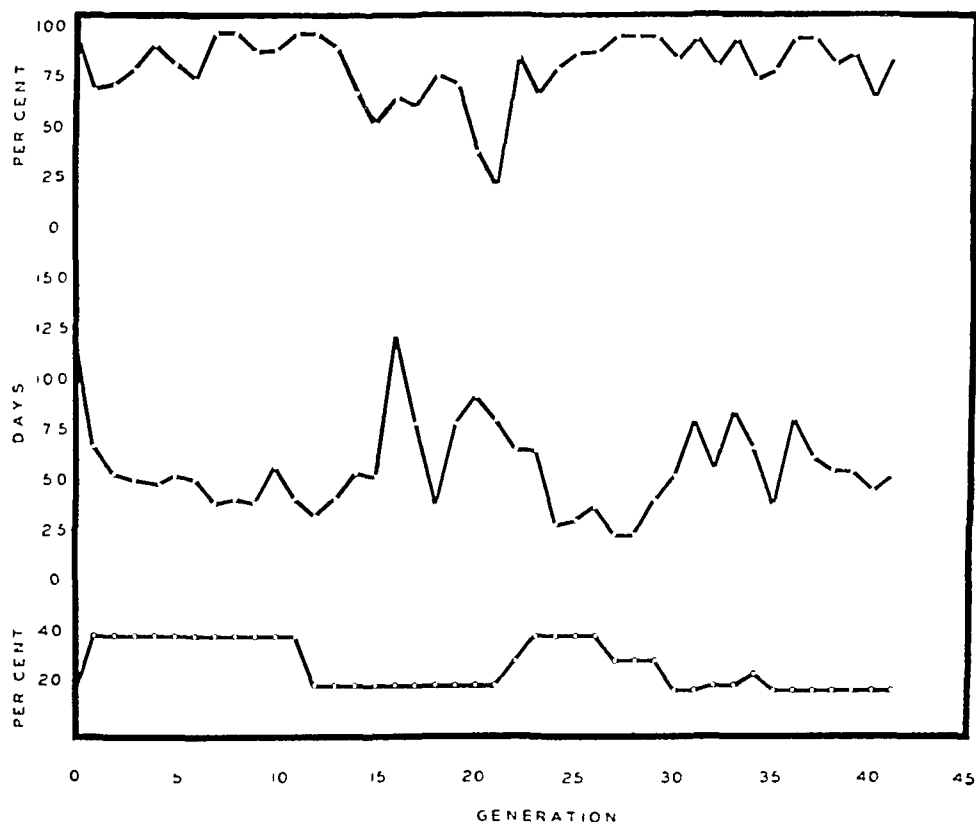


Fig 1—Chart showing increase in virulence of the virus of lymphogranuloma inguinale through successive passages in mice. The increase in virulence is evidenced by an increase in the mortality rate and a shortening of the period elapsing between inoculation and death relative to the concentration of inoculum used. The top line indicates the average mortality rate, the second line indicates the average period between inoculation and death, and the lowest line indicates the concentration of the inoculum.

short a period as two and six-tenths days (the inoculums used were slightly weaker than those of the first eleven passages) affords clear evidence of the increase in virulence of the virus of lymphogranuloma inguinale on passage in mice.

The mice used for the thirtieth and succeeding passages received inoculums of dilutions 1:5 to 1:6 suspended in Tyrode's solution, physiologic solution of sodium chloride buffered and unbuffered broth and ascitic fluid. There appeared to be little difference in the results obtained with any of these diluents. A com-



parison of the time elapsing between inoculation and death and the mortality rate with those of the twelfth to the twenty-first passage, in which approximately the same dilution of inoculum was used, affords further evidence that the virus had become "fixed" for the brains of mice

There was no reaction to intracerebral inoculation with a 40 per cent suspension of either normal mouse brain or lymphogranulomatous mouse brain heated to 60 C for three hours

Six hundred and eighty-three mice have been used in this work thus far. A series of 348 of these were given material 27 and the virus from its subpassages, and 335 were given material 28 and the virus from its subpassages. Eighty and two-tenths per cent of the former and 86.6 per cent of the latter died. From 15 to 20 per cent of all the inoculated animals recovered, although all were sick and many were desperately ill. Convalescence began, on the average, twelve days after inoculation, with a maximum and a minimum of thirty and four days, respectively. The animals had completely recovered, on the average, twelve days after the beginning of convalescence, with a maximum and a minimum of forty-one and two days, respectively.

*Frei Antigen*—In the preparation of Frei antigens from lymphogranulomatous brains, the series of mice receiving material 27 and virus from its subpassages was kept separate from the series receiving material 28 and virus from its subpassages and duplicate antigens were made from most inoculums. The results obtained with the two series have been identical.

In the case of the first twenty-three passages, the antigen and the inoculum were of the same concentration, ranging between 40 per cent and 20 per cent of virus-containing material. Beginning with the twenty-fourth passage, the concentration of antigenic material was reduced to 10 per cent owing to the severity of the reactions produced with the stronger suspension. The diluent for all antigens up to the thirty-third passage was a sterile buffered physiologic solution of sodium chloride. Antigens of succeeding passages were prepared with a sterile unbuffered physiologic solution of sodium chloride.

All the antigens prepared from mouse brains were tested in human subjects within one month after preparation, and those of the earlier passages were tested again from three to six months later. Of three antigens tested six months, two tested five months and twenty-two tested three months after preparation, none has shown any decrease in potency on standing.

The intensity of the Frei reaction in lymphogranulomatous human subjects produced by antigens prepared from mouse brains has increased with each successive passage in mice. Thus, intradermal inoculation with 0.1 cc of antigen prepared from the 40 per cent emulsions of the brains of mice used in virus of the first ten passages produced no stronger reaction than did 0.1 cc of Frei antigen prepared from pus from a human subject. For the twelfth to the twenty-first passage, inclusive, when the concentration of antigenic material was reduced to 20 per cent, or half that of the preceding ten passages, a reaction equal to that produced by antigen prepared from material from a human being was obtained with the use of only 0.05 cc. A further reduction in concentration of antigenic material to 10 per cent was introduced with the twenty-fourth passage, and the reactions produced by the use of 0.05 cc were slightly stronger than those produced by 0.1 cc of antigens prepared from the brains of mice used in the first ten passages. We

feel that these results can be interpreted quantitatively as approximately a four-fold increase in strength of antigenic material from the twelfth to the twenty-first passage and as an eightfold increase in subsequent passages. The increase in strength of the reaction to antigens prepared from mouse brains is shown by a larger surrounding area of erythema, a brighter scarlet zone surrounding the central papule, which frequently has a vesicular or pustular center and at times becomes necrotic.

As it was possible that the subject tested might react to the proteins of a normal mouse brain, control tests were made concurrently with the Frei tests, by using an emulsion prepared from normal mouse brain in the same concentration, and by the same methods, as the Frei antigen prepared from lymphogranulomatous mouse brain. Readings were taken of the reactions to emulsions prepared from lymphogranulomatous and from normal mouse brains at the end of forty-eight and seventy-two hours. The reactions produced with emulsions of lymphogranulomatous mouse brains in normal human subjects and with emulsions of normal mouse brains in all human subjects were insignificant at the end of seventy-two hours. None of the 143 tests made on twenty-two lymphogranulomatous human subjects or the 145 tests made on thirty-eight normal human subjects with antigens prepared from mouse brains has been found to cause untoward effects.

#### *Histopathologic Appearance of Lymphogranulomatous Mouse Brains*

—The histopathologic picture of the brains of mice dying as the result of intracerebral inoculation with the virus of lymphogranuloma inguinale was that of meningo-encephalitis. Examination was made of coronal and sagittal sections of the brains of twenty-eight mice which died between one and twenty-five days after inoculation. The same broad type of reaction was present in all the brains. There were, however, certain well defined differences in the types of cells noted, depending on the length of time that elapsed between inoculation and death. The pathologic changes observed were chiefly (1) exudate into the meninges and ventricular system with considerable vascular congestion, (2) formation of foci of inflammation and vascular congestion in the brain substance and (3) the presence of intracytoplasmic bodies.

The most outstanding and constant lesion was the exudate into the meninges and ventricular system. In the former it was confined largely to the pia mater and subarachnoid space and the septum passing into the brain substance. It was heaviest in the neighborhood of blood vessels and was usually associated with hemorrhage and the formation of fibrin. In the ventricular system it was uniformly distributed. Frequently, ependymal cells were found free in the ventricles, which was probably due to changes in the ventricular walls. No mitotic figures were observed in the ependyma.

The cells constituting the exudate were macrophages, polymorphonuclear leukocytes, plasmacytoid cells, a few lymphocytes, some multinucleated cells and a number of very large cells, possibly macrophages but somewhat resembling lymphoblasts, with dark nuclei and comparatively little cytoplasm. The macrophages appeared as large cells usually round or oval but sometimes showing short, blunt pseudopodia, with a large somewhat centrally placed nucleus. The nucleus was oval or slightly indented with a well marked nuclear membrane containing irregu-

larly distributed nodes of chromatin on the inner margin. More centrally, the chromatin was arranged in fine sparse strands and in small masses.

The proportions in which the different types of cells were found in the exudate varied with the length of time elapsing between inoculation and death. Thus, in a mouse that died twenty-four hours after inoculation only polymorphonuclear leukocytes and macrophages were present, in the proportion of approximately 90 and 10 per cent, respectively. In an animal that died after forty-eight hours the number of polymorphonuclears decreased to 70 per cent, and the number of macrophages increased to 30 per cent. As the time elapsing before death lengthened, the polymorphonuclears gradually disappeared and were replaced by macrophages and plasmacytoid cells, so that by the eleventh day the exudate was seen to consist of 15 per cent polymorphonuclears, 80 per cent macrophages and 5 per cent plasmacytoid cells. The plasmacytoid cells seemed to make an appearance at about the tenth day after inoculation. Twenty-five days between inoculation and death was the longest period of illness in any mouse studied. In the brain of this mouse it was observed that the macrophages, which at first replaced the polymorphonuclears, were themselves later partly replaced by plasmacytoid cells, for in this brain the proportions of polymorphonuclears, macrophages and plasmacytoid cells were 5, 30 and 65 per cent, respectively.

The plasmacytoid cells resembled very much those described by Findlay.<sup>1</sup> They were somewhat smaller than the macrophages, oval or pear-shaped, with a strongly acidophilic and somewhat vacuolated cytoplasm. The nuclei were usually round and smaller than those of the macrophage, and the chromatin was arranged in relatively heavy masses around the periphery. The arrangement of the chromatin did not have the well defined and regular spacing of that in the typical plasma cell, but the approximation was sufficiently close to render these cells easily distinguishable and to warrant the use of the term "plasmacytoid." Certain acidophilic cells, which may have belonged to this type, showed from two to four nuclei. It is interesting to note here that Findlay<sup>2</sup> and Levaditi and his associates<sup>3</sup> reported that plasmacytoid cells were numerous and polymorphonuclear leukocytes were rare in the brains of mice which died after inoculation with their strains of the virus of lymphogranuloma inguinale. This was probably due to the fact that the strains of virus employed by these workers required a longer time to kill the animals than did the strain we used.

Small lymphocytes, although they were few, were observed in all sections.

In late lesions, in the animals dying some time after inoculation, an anastomotic arrangement of the cells of the pia mater was noted, which resulted in a thickening of this membrane, producing the appearance of a proliferative leptomeningitis. It was notable that there was no marked subpial gliosis in the presence of the pial lesion. There was also well marked swelling of the walls of the capillaries and of some of the smaller arterioles, this swelling was of a hyaline nature and appeared to result in the complete blocking of some of the capillaries, which thus came to resemble giant cells in their appearance.

The foci of inflammation in the brain substance were present as cuffs of cells occupying, to a greater or less degree, the perivascular spaces of the smaller blood vessels, especially in the neighborhood of the ventricular system, and infrequently as single or multiple micro-abscesses. The cells composing the perivascular cuffs were of the same type as those in the meningeal exudate. Occasionally, swelling of the endothelial lining of the vessels which showed perivascular infiltration was observed. Micro-abscesses were well marked in five cases and varied in size from a cluster of about twenty polymorphonuclear leukocytes to a replacement of it



Fig. 2—Meningeal exudate from the base of the brain of a mouse that died two days after intracerebral inoculation with material from a mouse used in the thirty-second passage of the virus of lymphogranuloma inguinale. Note the distribution of polymorphonuclear leukocytes and macrophages. Sagittal section stained with hematexylin and eosin.  $\times 1450$

least one half of a coronal section of the cerebral hemispheres with these cells. One micro-abscess of moderate size involved both the meninges and the brain substance and was arranged around a large meningeal blood vessel.



Fig 3—Brain of a mouse that died six days after intracerebral inoculation with material from a mouse used in the second passage of the virus of lymphogranuloma inguinale. Exudate and detachment of the ependyma appear in the ventricle, and perivascular infiltration may be observed in the brain substance. Coronal section, stained with hematoxylin and eosin,  $\times 105$ .

Only three brains of the twenty-eight studied showed the presence of intracytoplasmic bodies. The bodies appeared extracellularly as well as intracellularly.

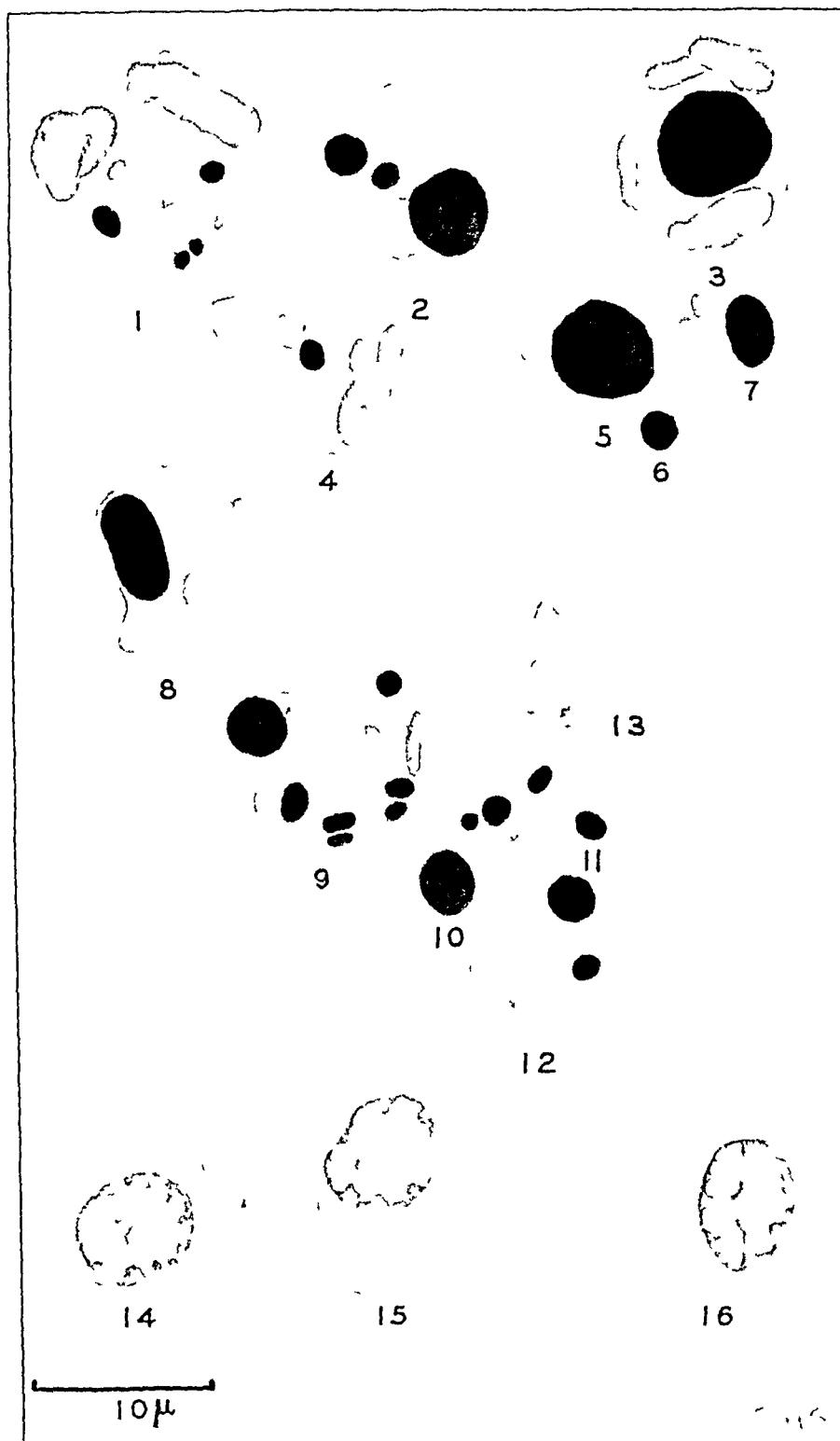


Fig 4—Intracytoplasmic bodies and plasmacytoid cells noted in lymphogranulomatous mouse brains (hematoxylin and eosin stain) 1, 3, 4 and 9 are cells seen in a micro-abscess containing intracytoplasmic bodies and remains of nuclei, 2, 5, 8, 12 and 13 are cells seen in a micro-abscess which contained intracytoplasmic bodies but in which nuclei had entirely disappeared, 6, 7, 10 and 11 are extracellular bodies, 14, 15 and 16 are plasmacytoid cells noted in exudate into the ventricular system of the brain of a mouse that died twenty-five days after inoculation

and assumed a deep red in sections stained with hematoxylin and eosin. They varied in size from 1 to 4 microns in diameter, the smallest particles being mere spicules. They appeared homogenous in consistency, and in none could any definite structure be detected.

When the bodies were encountered intracellularly, the cells in which they were found usually contained little typically staining nuclear material. In most cases, the nucleus had disappeared, and in the remainder it was represented by a more or less narrow rim of chromatin toward the periphery of the cell. Because of this, identification of the type of cell in which the bodies were included could not be made. They were observed only in the presence of an intense polymorphonuclear reaction and were most marked in the largest microabscess of the brain substance.

On the whole, the appearance and distribution of the intracytoplasmic bodies coincided fairly well with the description given first by Favre<sup>7</sup> of those found in buboes and later by Findlay<sup>8</sup> of those seen in lymphogranulomatous brains.

#### SUMMARY AND CONCLUSIONS

A strain of the virus of lymphogranuloma inguinale obtained from the pus and glandular material of a patient presenting the inguinal type of the disease has been successively transmitted in mice by intracerebral inoculation for forty-one passages (at the time of writing).

The virus increased in virulence with successive passages in mice.

Lymphogranulomatous mouse brains provided a readily available source of specific Frei antigen, the potency of which increased with successive passages.

Frei antigens prepared from mouse brains were tested six months after preparation and found to retain their potency for at least that length of time.

Emulsions of normal mouse brains prepared and tested in the same way as Frei antigen did not produce any appreciable reaction.

In the 143 Frei tests done on twenty-two lymphogranulomatous human subjects and the 145 tests done on thirty-eight normal human subjects, no untoward effects were caused by the use of material prepared from mouse brains.

The brains of mice which died from an intracerebral inoculation of the virus of lymphogranuloma inguinale showed meningo-encephalitis on histologic examination. Exudate into the meninges and ventricular system and perivascular infiltration with infrequent formation of abscesses in the brain substance were the chief lesions.

The inflammatory cells consisted of polymorphonuclear leukocytes, macrophages, plasmacytoid cells, a few small lymphocytes and a number of very large cells, possibly macrophages. The proportion in which the cells of the first three types occurred depended on the length of time that elapsed between inoculation and death.

Intracytoplasmic bodies were encountered infrequently.

<sup>7</sup> Favre, M. Sur l'etiologie de la lymphogranulomatose inguinale subaiguë (Ulceré vénérien adénogène). *Presse med* 32: 651 (Aug. 2) 1924.

# TRANSFORMATION OF TRICHOPHYTON GYPSEUM INTO MOSAIC FUNGUS

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When epidermal scales parasitized by ringworm fungi are cleared in potassium hydroxide and examined microscopically, there is frequently found, in addition to the normal mycelium of the parasite, a network of disorganized material described in the literature as the "mosaic fungus"

There is difference of opinion as to the nature of the mosaic fungus. It was first described by Weidman<sup>1</sup> who pointed out that it follows the outline of the walls of the epidermal cells in such a way as to suggest that an or some other refractile matter is imprisoned between the cells. He succeeded in separating the mosaic fungus from the cells by microdissection and in staining it with Giemsa's stain, and he concluded from this that it is of fungous nature. Greenwood and Rockwood<sup>2</sup> stated that they had observed the mosaic fungus in contact with normal hyphae and concluded that it is disintegrated fungous material. Becker and Ritchie<sup>3</sup> observed the mosaic and a true fungus in the same preparation, but careful microscopic examination convinced them that the two were not in contact. They stated that the mosaic fungus is the result of inflammatory changes in the tissue. Similarly Bruhns and Alexander<sup>4</sup> expressed the view that the so-called mosaic fungus is not of fungous origin. MacKee and Lewis<sup>5</sup> weighed the evidence in favor of the mosaic formation being a fungus as against that in favor of its being an artefact. They stated that (1) patients with the mosaic fungus in

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1 Weidman F D. Laboratory Aspects of Epidermophytosis, *Arch Dermat & Syph* **15** 415 (April) 1927

2 Greenwood A M and Rockwood E M. The Skin in Diabetic Patients, *Arch Dermat & Syph* **21** 96 (Jan) 1930

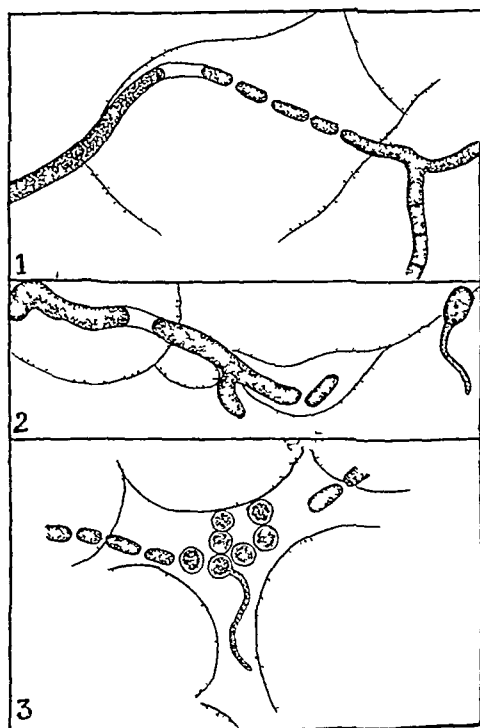
3 Becker S W and Ritchie E B. The Role of Yeasts in the Production of Superficial Dermatitis. *Arch Dermat & Syph* **22** 790 (Nov) 1930

4 Bruhns C and Alexander A, in Jadassohn I. *Handbuch der Haut- und Geschlechtskrankheiten* Berlin Julius Springer 1928 vol 11 pp 89 and 464

5 MacKee G M and Lewis G M. Keratolysis Foliativa and the Mosaic Fungus. *Arch Dermat & Syph* **23** 445 (March) 1931



the epidermal tissue always have a history of mycosis, (2) normal fungus mycelium is frequently present in the same tissue as the mosaic fungus and (3) skin from experimentally produced blisters on patients free from mycosis contains no such mosaic formations. On the other hand, they expressed the opinion that (1) the mosaic fungus is unlike a normal fungus in that it is irregular in contour and (2) it has never been known to grow on culture mediums. The authors come to the conclusion that the mosaic formation is a disintegrated fungus. Cremer,<sup>6</sup> after examining 100 patients with the mosaic fungus in the epidermal scales, decided that it is not fungous tissue. Recently Davidson and Gregory<sup>7</sup> observed



Figs 1-3—Potassium hydroxide preparations of skin from a lesion on the thumb of Mr. P. at an early stage of the infection, showing mycelium and spores of *T. gypsum* ( $\times 350$ ). Figure 1 shows spore formation, figures 2 and 3, spore germination.

that the mosaic fungus is made up of flat rhombic crystals, which they identified as cholesterol. They consider that in the light of the present knowledge of the subject the presence of the mosaic fungus cannot be regarded as evidence of fungous infection.

6 Cremer, G. Untersuchungen über die Epidermophytie der Füße und Hände in Amsterdam, *Arch. f. Dermat. u. Syph.* **169**:244, 1933.

7 Davidson, A. M., and Gregory, P. H. The So-Called Mosaic Fungus as an Intercellular Deposit of Cholesterol Crystals, *J. A. M. A.* **105**:1262 (Oct 19) 1935.

It is common to find skin containing only the mosaic fungus and no normal fungus. Because of the general disagreement in the literature as to the nature of the mosaic fungus, one cannot satisfactorily interpret such findings. Consequently, it seemed advisable to carry out further studies on the subject.

#### METHOD OF STUDY

In order to demonstrate fungi or mosaic fungi in suspected lesions of the skin or in the hair, the tissue was immersed in an 8 per cent solution of potassium hydroxide for about fifteen minutes, or until the preparation was transparent, and then it was examined microscopically.

Our findings were based on the study of material collected from twelve patients suffering from diseases clinically diagnosed as dermatomycosis. In all twelve patients the mosaic fungus was demonstrated, but in only six of them were we able to demonstrate the living fungus microscopically and by culture.

The investigation of the relation between the living mycelium and the mosaic fungus was carried out as follows. The mycelium was cultured on Sabouraud's medium and identified, a study was made of the fungus as it occurred in the infected tissue, especially when it was in a disorganizing or sporulating condition. A morphologic study was made of the mosaic fungus, in tissue in which a normal and the mosaic fungus were associated, a comparison of the two structures was made, and the tissue was searched with a view to discovering any intermediate forms or any actual contact between the two.

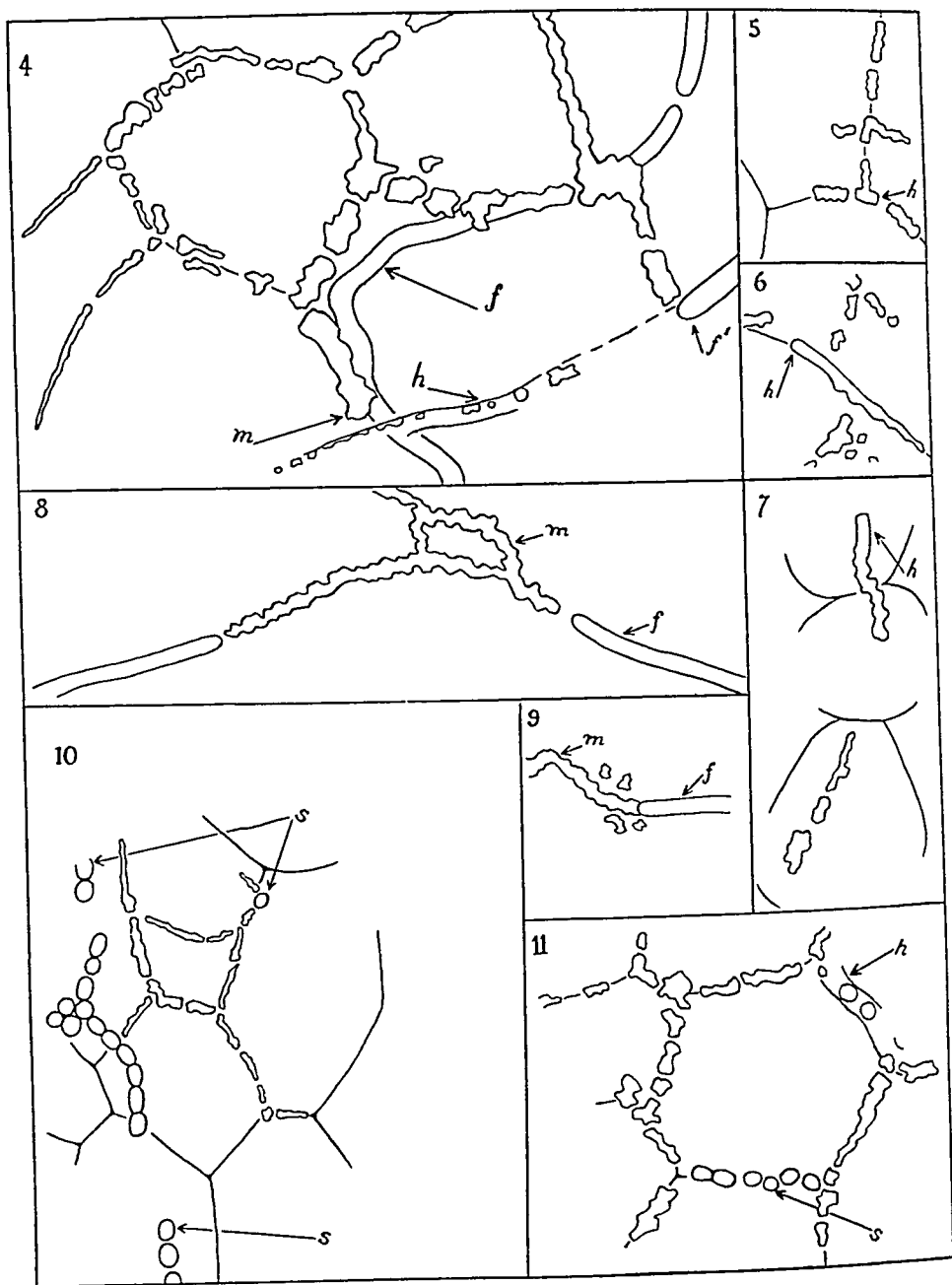
#### CULTURAL FINDINGS

Material from four patients having lesions which contained the mosaic fungus and no living fungus was planted on slants of Sabouraud's medium, and no fungus growth appeared in any of the tubes. On the other hand, mycelia were readily obtained on Sabouraud's medium when scales which contained both mosaic and normal hyphae were used as inocula, and in this manner growths were obtained from the cutaneous tissue of six patients with mycotic lesions. Each of the six growths was identified as *Trichophyton gypsum*, having the following characteristics on Sabouraud's medium. The mycelia were silky and white at first, later becoming granular in texture and deepening to "light buff"<sup>8</sup>. One culture was tinged with pink during the second week of its growth but later became buff like the others. All the cultures possessed spiral racquet hyphae, chlamydospores, aleuriospores and fuseaux. The walls of the hyphae and of the spores in some strains were slightly torulose and in one strain were remarkably so. In all the fuseaux were clavate thin-walled and from one to six septate, their average length being 30 microns.

It is well known that one species of fungus may be the cause of a variety of clinical manifestations of mycosis. We have cultured

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<sup>8</sup> Ridgway, R. Color Standards and Color Nomenclature, Washington, D. C. The Author, 1912.

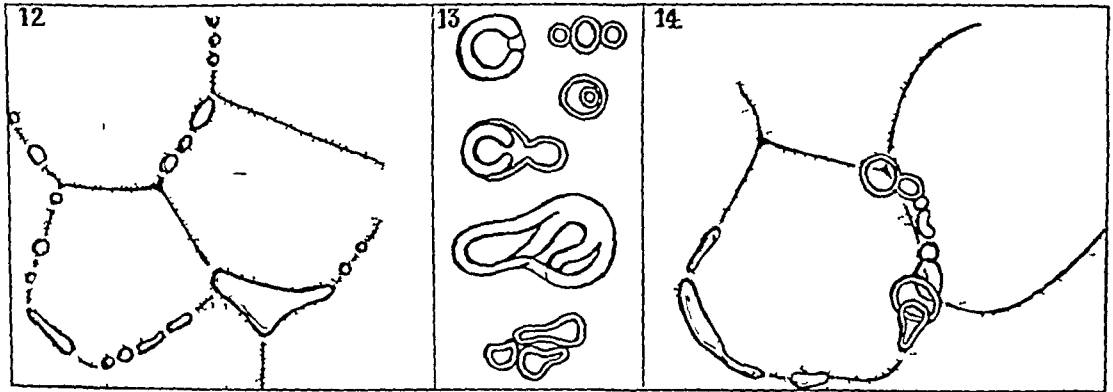


Figs 4-11—Potassium hydroxide preparations of skin containing mosaic fungus taken from lesions of patients with mycosis. The magnification of figure 4 is about 500, that of the other figures, 250. Figure 4, from a lesion on the foot of Miss M, shows the active fungus, *f*, and the mosaic, *m*, in the same field. The hypha at the lower right, *f*, has disorganized at *h*. The wall of the cell is disappearing and the drops of oil and mosaic segments are left behind. Figures 5 to 7 show hyphal remnants, *h*, from foot of Miss S in the mosaic formation. In figures 8 and 9, from the foot of Miss M, the mosaic fungus, *m*, is a continuation of the active hypha, *f*. In figure 9 the two are in actual contact. Figures 10 and 11, from the thumb of Mr P, show the mosaic fungus containing normal fungous spores, *s*, and a disintegrating hypha, *h*, with drops of oil.

T gypsum from deep-seated pustular lesions of the glabrous skin and of the beard, and from superficial dry, scaling lesions of the hands and feet. Similarly, we have observed the mosaic fungus in these same lesions, sometimes in close association with the normal fungus.

#### IN SITU FINDINGS

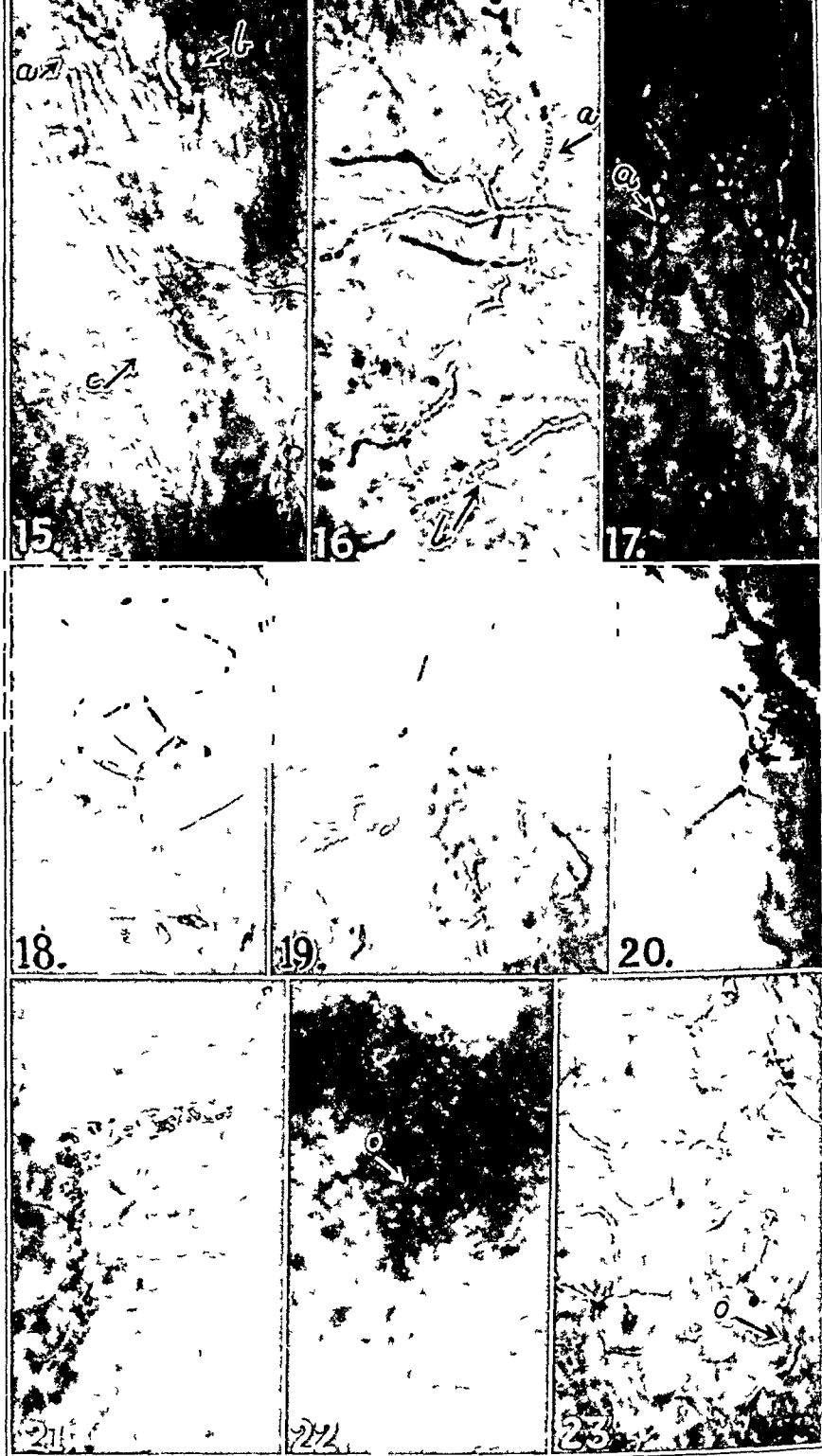
*T. Gypsum in the Skin*—In our preparations *T. gypsum* appeared as an intercellular parasite with a branched septate mycelium averaging 6 microns in width. In its early vegetative condition it grows comparatively straight. The hyphae of what are taken to be the older established mycelia curve about between the cells and tend to form a reticulum. At this stage spores form by the segmentation of the hyphae after the manner of oidia (figs 1, 15 and 16). Septums form at more frequent intervals than in the vegetative mycelium, about 10 microns apart. From what can be made out in the potassium hydroxide prepara-



Figs. 12-14—Skin from lesions free from fungi, showing oil globules simulating the mosaic fungus ( $\times 325$ )

tions, it seems that the protoplasm then shrinks from the septums and forms new curved walls about itself. The rows of spores are then set free by the disorganization of the primary septums. In our preparations some spores were germinating and had sent out narrow germ tubes growing at right angles to the row of spores and between epidermal cells (figs 2 and 3).

When skin is invaded by mycelium it contains a proportion of dead fungous tissue. One or two cells here and there disintegrate and break up the parent hypha into a system of dissociated segments (fig 16 *b*), or the parasite fades throughout the length of one or several hyphae (fig 15 *a*). The steps in the process of disorganization seem to be as follows: 1. Oil globules appear in the cytoplasm of the older living hyphae. 2. The globules enlarge until they approach the diameter of the hyphae when they may resemble rows of endospores. 3. The cell walls fade out so that rows of globules replace the dead hyphae.



Figs 15-23—Figures 15 to 17 show epidermal tissue in prepared potassium hydroxide ( $\times 325$ ). In figure 15, the hair of the beard, infected with *T. gypseum*, is dissolved away to show mycelium *a*, spores, *b*, dead cell, *c*, dead hypha with drops of oil. Figures 16 and 17 show epidermal scales parasitized by *T. gypseum*. *a*, spores; *b*, cell separated from hyphae by the adjoining dead cells; figures 18 to 20, epidermal scales with the mosaic fungus. Figure 21 shows debris resembling the mosaic fungus in healthy skin. Figures 22 and 23 show artefacts due to intercellular inclusions of oil, *o*, in healthy skin.

4 Some of the globules are converted into angular retracting segments, and these constitute the mosaic fungus (figs 4 and 11 *h*) During this process the septums separating the living cell from the disorganized cell or cells, originally plane, become bulged with the convex surfaces toward the dead cell (fig 15 *b*), as described by Buller<sup>9</sup> in his experiments on wounding hyphal cells

*T. Gypsum in the Hair*—The mycelium produces a greater abundance of spores in the hair of the beard than in the skin The hairs are sheathed with rows of spores, as is typical of hairs infected by ectothrix trichophytons Within the hair a branched septate mycelium grows longitudinally Spores are formed as in the skin by the breaking up of the hyphae into oidia (fig 15) Hyphae or hyphal segments frequently die, and the cell walls gradually disappear as they do in the skin, leaving rows of drops (fig 15 *c*), but we have never seen actual mosaic elements in the hair

*The Mosaic Fungus and T. Gypseum*—There can be no uncertainty as to the presence or absence of the mosaic fungus in specimens prepared for microscopic study, because when present it stands out sharply even under a low power lens (figs 19, 20 and 21) It occurs in patches in the skin, each patch being composed of a reticulum of a shiny substance which follows the outline of the epidermal cells The network is not continuous but is broken up into a linear arrangement of short oblong segments which are separated from one another The segments are of a fairly constant diameter about 8 microns, and their length is from 10 to 20 microns Their outline is angular rather than rounded, and their surface appears fissured

In preparations in which hyphae of *T. gypseum* and the mosaic fungus can be seen in the same field, we have observed the two in actual end-to-end contact so that the mosaic is a natural continuation of the hypha (fig 9) A septum convex on the surface opposed to the mosaic fungus, separates the two When the mosaic fungus is associated with *T.* hyphae it is more usual to find a slight separation between them—a space of at least 4 microns between the convex septum of the active hypha and the end of the mosaic formation Some hyphae have been found which had been converted to the mosaic form at one end, and others in which the middle was changed to the mosaic form and the two ends were normal (fig 8)

Within the mosaic fungus itself one may observe parts which betray a fungous origin Fungous spores are frequently found making up part of the mosaic fungus (figs 10 and 11 *e*) It is probable that the spores are particularly resistant to the reaction of the host cells The

<sup>9</sup> Buller A. H. R. *Researches on Fungi* New York Longmans Green & Co. 1933 vol. 5 p. 313

faint outline of the walls of hyphae may also be seen, the oil globules derived from their contents contributing to the mosaic complex (figs 4 and 11 *h*) Some mosaic segments are not flattened like the rest but retain their cylindric shape and are indistinguishable from normal hyphae (figs 5, 6 and 7)

*The Mosaic Fungus in Healing Lesions*—The mosaic fungus is sometimes observed in healing lesions, as illustrated by the following case

Mr P, a farmer, was admitted to the University Hospital on March 8, 1933, suffering from mycosis of the beard, upper lid, left eyelid and left thumb On admission, fungi were demonstrated microscopically in the hair of the beard, and fungous mycelium and a mosaic fungus were observed in epidermal scales from the thumb Both hairs and scales, when sown on Sabouraud's medium, gave rise to a growth of *T. gypseum* On March 12, there developed a generalized trichophyoid eruption, consisting of closely aggregated papules the size of a pinhead and each surmounted by a tiny pustule No fungi could be demonstrated in these lesions, and the blood of the patient was cultured for fungi without success Daily examinations of material from this patient demonstrated very clearly that as healing proceeded active fungi became less obvious and the mosaic fungus more prominent, until in the majority of the scales only the mosaic fungus could be demonstrated

*Artefacts Simulating the Mosaic Fungus*—When healthy or parasitized epidermal tissue is examined microscopically, structures other than the mosaic form will be found that could be mistaken for fungous hyphae Frequently debris from ointment or other foreign substances is plentiful in the scale to be examined (fig 21) The solid particles often lodge in the intercellular spaces, so that under the low power lens of the microscope a reticulum of small brown particles can be found throughout the tissue, looking very similar to the mosaic fungus The particles can, however, be distinguished from the mosaic fungus by careful examination

Another common mosaic-like artefact found both in healthy skin and in skin infected by fungi is oil Drops of oil may be left in the tissue after the disorganization of the hypha of a dermatophyte, but more frequently they are not of fungous origin (figs 12 and 23)

The oil globules may be double-contoured and adhering together, closely resembling fungi (figs 13 14 and 22) Becker and Ritchie<sup>9</sup> observed in potassium hydroxide preparations of skin yeastlike and hypha-like bodies which were round or oval and double-contoured, with no contents They considered them artefacts due to potassium hydroxide Finnerud<sup>10</sup> observed ovoid or budding "cells" from 2 to 3 microns in diameter some single some double-contoured, occurring especially

<sup>10</sup> Finnerud C W Perleche A Clinical and Etiologic Study of One Hundred Cases Arch Dermat & Syph 20 454 (Oct) 1929

between the epidermal cells. He photographed these as a possible cause of perleche but expressed some doubt as to their nature.

The same bodies have been observed in specimens of tissue taken from our patients. They occur between the cells separately, in chains or in clusters and consist of single-contoured or double-contoured bodies of a variety of shapes—spherical, ovoid or elongate—frequently with smaller bodies attached as though the larger one had formed a bud. Examination with Nicol's crossed prisms shows the bodies to be doubly refractile, indicating that they are probably drops of oil. When these occur between epidermal cells, they might easily be taken for the mosaic fungus unless one were thoroughly familiar with the appearance of the mosaic fungus. The drops of oil differ from the mosaic segments in that they do not stand out clearly and are visible only under a carefully focused high power lens and that they are smooth and rounded in outline, never angular.

#### SUMMARY

Skin from mycotic lesions of patients usually contains, in addition to the normal fungous parasite, a network of disorganized material known as the "mosaic fungus."

Frequently skin contains no normal mycelium but only the mosaic fungus. In such tissue it is particularly necessary to come to a conclusion as to whether or not the mosaic formation is of fungous origin.

When skin examined in the University of Alberta Hospital contained both mosaic and living fungi, growths of *T. gypseum* were obtained from the skin in culture.

*T. gypseum* mycelium in the skin frequently disorganizes. When the wall of the fungous cell dissolves a row of oil globules is left in the tissue, these may take on the form of angular refractile segments, the mosaic fungus.

The following evidence goes to show that the mosaic fungus is of fungous origin. 1. Mosaic segments have been observed in tissue joined end-to-end with *T. gypseum* hyphae and also close to the ends of the hyphae but not in actual contact. 2. Normal fungous spores and traces of fungous hyphae have been observed making up part of the mosaic formation. 3. It was found that during the healing of lesions of a patient suffering from *T. gypseum* infection the mosaic fungus increased and the living fungus decreased.

Criteria are given by which to distinguish between the mosaic fungus and substances which are not of fungous origin but are similar in appearance to the mosaic fungus.



# FATALITY FOLLOWING BISMARSEN THERAPY

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Since the use of bismarsen in antisyphilitic therapy there have been numerous reports on the various types of untoward reactions encountered, but a search of the literature reveals no report of fat embolism as a complication. We therefore believe that the following case merits record.

## REPORT OF A CASE

P S, a 47 year old salesman, married, was referred to the dermatologic clinic from the medical department because of a positive Wassermann reaction found on routine examination. The patient had had hypertension for years.

On questioning the patient gave the following history. Twenty-four years before he had had a gonorrheal infection. Two years later he had had a penile sore followed by a rash. The Wassermann reaction was reported positive. He then received oral medication. Three years before admission to the clinic his Wassermann reaction was found to be positive at another clinic, and he was given twelve intravenous injections. The Wassermann reaction was reported negative following these injections, and he therefore discontinued treatment.

His wife was living and well. The first pregnancy had resulted in a miscarriage. One child 14 years of age, was living and well. There were no other pregnancies.

Physical examination showed a well developed, well nourished middle-aged man, slightly cyanotic. The pupils were equal and reacted to light and in accommodation. Culture of material from the mouth and throat gave negative results. The lungs were resonant. The area of cardiac dullness extended 10.5 cm to the left of the midsternal line and supracardiac dullness extended for 6.5 cm. A soft systolic murmur was audible at the apex, and there were many premature beats. The abdomen and reflexes were normal.

*Laboratory Data*—The Wassermann and Kahn reactions were positive. The spinal fluid showed a positive Wassermann reaction. The globulin and total protein contents and the colloidal gold curve were normal.

The patient received a course of fourteen intramuscular injections of a bismuth preparation (quinine bismuth iodide, 0.2 Gm). After that he was given intravenous injections of neoarsphenamine, 0.45 Gm. After the third injection of neoarsphenamine the patient complained of itching but showed no eruption. The sclerae were then slightly yellow. The skin was normal. The administration of neoarsphenamine was discontinued. For the next four weeks the patient received no treatment. The

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From the Department of Dermatology and Pathology at the Beth Israel Hospital.

jaundice and itching completely cleared. He was then given tryparsamide (dose 2 Gm). After twenty-five injections the spinal fluid was examined and found to be completely normal. The reactions of the blood, however, were still positive. The patient was therefore given intramuscular injections of bismarsen on the basis that this combination would be beneficial if he could tolerate it. After the second injection of 0.2 Gm the patient stated that he felt "sick" all week but had no definite symptoms. Immediately after the third injection the patient became weak and pale, felt nauseated and vomited. He had a chill and complained of backache. He was immediately placed on his back and covered with blankets. His skin was cold and clammy, the pulse was rapid and feeble. Epinephrine (0.5 cc) was administered. Within a few hours the patient became markedly jaundiced. The blood pressure was 150 systolic and 100 diastolic. The lungs were clear. The abdomen was soft and nontender. The reflexes were normal. Over both lower extremities numerous pinpoint purpuric spots were observed.

The urine was dark red, had a specific gravity of 1.030 and showed a large trace of albumin, the presence of bile, a 4 plus reaction to the guaiac test and a normal sediment. The results of further laboratory studies (about twelve hours after the injection) are as follows: red blood cells, from 5,200,000 to 4,350,000, hemoglobin, from 65 to 75 per cent (Tallqvist), white blood cells, from 26,000 to 17,800, nonprotein nitrogen 102 mg, creatinine 4.2 mg, plasma fibrinogen, 0.25 Gm, urea nitrogen, 49 mg, per hundred cubic centimeters, icteric index from 75 to 125.

Results of the Kahn, Hinton and Wassermann tests were negative. (It was interesting to see the serologic change with this marked reaction. This confirms previous similar reports.)

The patient's temperature gradually rose, the pulse rate ranged about 100 and the respiratory rate about 40. He remained in this condition, and death ensued within twenty hours from the time of the injection.

*Pathologic Changes*—Macroscopic Examination. Autopsy revealed a well developed and well nourished man, who showed marked generalized jaundice. Miliary petechiae were observed along the medial border of the left ankle and over the dorsum and instep of the right foot. There were a few smooth thin, inelastic areas of yellowish to deep brown discoloration over the shaft of the penis.

The subcutaneous fat was deep golden yellow, while the abdominal muscles although well developed, were paler and softer in consistency than normal.

The right pleural cavity contained 150 cc and the left 55 cc of amber-colored limpid serous fluid. There were firm fibrous apical adhesions bilaterally. No petechiae were seen.

A few petechiae were noted over the visceral pericardium. None were seen on the parietal pericardium.

The heart weighed 600 Gm. There was a well healed aneurysm of the wall of the heart near the apex measuring 6 by 7 cm and complete calcific occlusion of the descending branch of the left coronary artery. There was no evidence of recent thrombosis of the coronary arteries or of myocardial infarction.

The right lung weighed 400 Gm and the left 380 Gm. Beyond considerable posterior and dependent congestion macroscopic examination yielded no positive findings. No gross fat was visible in the larger blood vessels.

The spleen weighed 610 Gm and was of very firm consistency. There was no evidence of infarction.

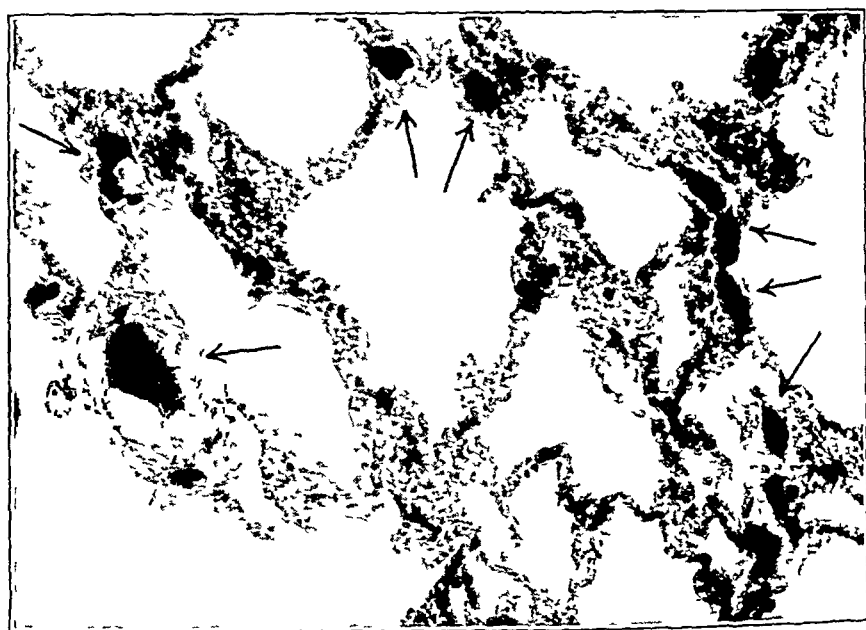
The liver weighed 1740 Gm. It possessed its usual size, lobulation and shape and was yellowish brown. The capsule was smooth and shiny. The liver was somewhat softer in consistency than normal. The usual hepatic markings were

distinguished without much difficulty. There was not a large amount of blood in the liver. The cut surface was moist and shiny, and the knife seemed to be slightly greased as the section was made.

The gallbladder was of moderate size, dark green and slightly distended, with a moderate amount of thick dark green bile, some of which could be expressed through the ampulla of Vater. There was a small, firm, dark brown stone in the neck of the gallbladder, which did not obstruct the outflow of bile. No stones were found in the cystic or hepatic ducts or the common bile duct.

The right kidney weighed 220 Gm and the left 200 Gm. The only gross variation from the normal appearance was the lack of normal differentiation between the cortex and the medulla, the cut surface was a uniform purplish pink.

In the aorta numerous projecting patches of pale blue hyalinized thickened intima were observed, some showed atheroma and others calcification. These were



Photomicrograph (low power) showing fat embolism in the lung. The tissue was fixed with Zenker's fluid and stained with scarlet red and alum hematoxylin. The arrows indicate pulmonary capillaries distended with plugs of fat which stained a deep orange. Similar emboli were seen in the capillaries of the glomerular tufts.

scattered over the entire extent of the aorta. Between the patches there were areas of retraction of the intima, producing stellate and parallel depressed lines. Two centimeters from the aortic ring a dilatation of the ascending aorta was observed. Considerable "tree barking" and ulceration were noted in the region of the bifurcation.

The gastro-intestinal tract, pancreas, adrenal glands, bladder, genitalia, organs of the neck and bone marrow were normal.

The brain weighed 1,320 Gm. It was symmetrical, and the convolutions and sulci stood out well. There were no areas of softening or induration. The fluid in the cisterna magna was bile-tinged. The leptomeninges were not thickened.

The vessels at the base of the brain showed some evidence of irregular thickening, but no aneurysms were present. Transverse sections made after fixation in formaldehyde showed no evidence of hemorrhagic encephalitis.

**Microscopic Examination** Microscopic examination of the heart confirmed the gross finding of a well healed cardiac infarction. There was no evidence of acute infarction.

Study of numerous sections taken from all the lobes of the lungs showed the presence of numerous clear, nonstaining areas within the alveolar walls giving them a somewhat beaded appearance. In some places these areas were lined with endothelium and in others they were not, they contained no blood cells. Numerous sections stained with scarlet red (fig 1) showed these areas to be fat droplets of variable size. Every field studied was loaded with such deep red, tortuous and branching areas, for the most part lined by endothelium. As these branches conformed to the usual shape of the capillaries, it was concluded that they represented intracapillary emboli.

The spleen showed a recent hemorrhagic infarct.

In addition to a rather dense focal lymphocytic infiltration in the periportal spaces of the liver, there was a very slight degree of fatty infiltration of the liver cells, in the form of fine, nonstaining intracellular droplets. This was more marked in the central portion of the hepatic lobules than peripherally. These fatty changes were not marked, and the liver cells did not appear to be necrotic, the nuclei staining well and the hepatic lobular architecture being well maintained. No fat emboli were seen in the sinusoids.

The kidneys showed patchy arteriosclerotic changes. Many of the glomerular tufts showed numerous small, beaded, clear intracapillary droplets. A stain for fat showed them to be embolic plugs of fat. About four fifths of the glomeruli contained at least one tiny globule. The convoluted tubules showed some fatty changes.

There was marked perivascular round cell infiltration in the adventitia of the aorta. Numerous scars extended from the adventitia into the substance of the media, in which they distorted the structure of the media and the deeper layers of the intima.

In the brain fat embolism or hemorrhagic changes were not noted.

Under a low power lens bits of marrow interspersed with a great many red blood cells were seen. Under a high power lens the ratio of nucleated red cells to white cells was 1 to 0.66. The differential count of the white cells showed mature polymorphonuclears 1 per cent, metamyelocytes 13 per cent, myelocytes 52 per cent and occasional megakaryocytes.

The anatomic diagnosis was (1) syphilitic aortitis with dilatation, (2) healed cardiac infarct, (3) bilateral hydrothorax, (4) generalized jaundice, (5) cholelithiasis with pericholangitis, (6) hemorrhagic infarct of the spleen, (7) fat embolism of the lungs and (8) fat embolism of the kidneys.

#### COMMENT

While at the time of the autopsy it was believed that subsequent microscopic examination would show marked toxic changes in the liver, study of the finished sections yielded rather startling and upsetting findings. In the first place the fatty changes in the liver were not pronounced there being only periportal lymphocytic infiltration and relatively insignificant infiltration of the liver cells of the central portion.

of the lobule. It was difficult to believe that these changes brought about the abrupt and severe grade of jaundice which developed. Although stones were found in the gallbladder, there was no intrinsic or extrinsic obstruction of the biliary tract. The myocardial scar was similar to those noted occasionally at autopsy on patients who died of other causes, and because there was no recent infarction it seemed unlikely that the patient's death could be accounted for on this basis.

The fat embolism of the lungs, on the other hand, was so widespread that it alone may be considered as adequate to explain the fatal outcome. By effectively plugging the pulmonary capillaries, the fat emboli produced what Warthin referred to as the respiratory symptom and pathologic complex of fat embolism. It must be pointed out that fat embolism can be very easily missed on both macroscopic and microscopic examination. There may be absolutely no suggestion of the existence of the condition at autopsy, and with a hasty microscopic examination one can easily overlook the nonstaining droplets in sections stained in the routine manner. A special stain for fat is necessary to establish the diagnosis.

A comprehensive discussion of the subject of fat embolism will not be attempted here. The reader is referred to the excellent monographs of Warthin<sup>1</sup> and Landois<sup>2</sup> and the recent paper of Wright<sup>3</sup>. Suffice it to say, the condition is met with in three major conditions: (a) traumatic, for example, after fractures of bones or orthopedic manipulation, especially of atrophic, disused bones, (b) metabolic, as in diabetes, chronic nephritis, pancreatitis, chronic tuberculosis and acute and chronic alcoholism, and (c) toxic, as following the administration of chloroform, ether, carbon monoxide, alcohol, potassium chlorate,<sup>3</sup> phosphorus<sup>4</sup> and carbon tetrachloride.<sup>3</sup> It is remarkable that most of the drugs the use of which has been reported as leading to the development of fat embolism have a notoriously toxic action on the liver. However, no relationship between the damage to the liver and the fat embolism has been definitely established, and the true *modus operandi* of these drugs in causing fat embolism is not known.

With general reference to the category of toxic causes of fat embolism and with special reference to the present case, there are two recently reported fatalities from fat embolism following arsenic therapy.

1 Warthin A. S. Traumatic Lipemia and Fatty Embolism, *Internat Clin* **4** 171, 1913.

2 Landois Felix. Die Fettembolie, *Ergebn d Chir u Orthop* **16** 99 1923.

3 Wright, R. B. Fat Embolism, *Ann Surg* **96** 75, 1932.

4 Carrara M. Contributo statistico alla embolia adiposa polmonare nei suoi rapporti con la medicina legale, *Gior di med leg* **4** 209, 1897, German translation in *Bl f gerichtl Med* **49** 241 1898. Puppe G. Ueber Fettembolie bei Phosphorvergiftung. *Vrtljschr f gerichtl Med (supp)* **12** 95, 1896.

for syphilis. The first was reported by Burns and Bromberg in 1930.<sup>5</sup> The patient became ill immediately after an injection of a therapeutic dose of arsphenamine and died four days later. It was believed clinically that her death was due to arsphenamine poisoning. There was advanced mitral stenosis associated with cardiac enlargement and mild decompensation. In Burns and Bromberg's case the lungs showed no gross changes. There were multiple petechial hemorrhages throughout the white matter of the brain. Microscopic study showed that nearly all the pulmonary blood vessels were plugged with fat. The liver showed some small fatty droplets in the central portions of the lobules, but they were of limited distribution. A few isolated fat droplets were seen in the hepatic sinusoids. Fat emboli were found in the glomerular capillaries and in the nonhemorrhagic gray matter of the brain as well as in the centers of the hemorrhagic areas in the white matter. No description of the bone marrow was given. The authors made no attempt to explain the origin of the fat embolism in this instance. A second case was reported by Brittingham and Phinzy<sup>6</sup> in 1931. The patient showed the clinicopathologic syndrome of hemorrhagic encephalitis after the administration of neoarsphenamine. In all the sections of the brain, lungs, heart, liver, spleen, adrenal glands, kidney and pancreas, the capillaries were filled with fat. The condition of the bone marrow was not described.

It has been demonstrated that it is the arsphenamine radical<sup>7</sup> common to bismarsen and to the other arsenic compounds which is responsible for the untoward reactions occurring during treatment. We therefore believe that the present case is of the same type as those reported by the aforementioned authors.

#### SUMMARY

A case of fat embolism following the use of bismarsen is reported. A complete pathologic report and comment are given.

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5 Burns, E. L., and Bromberg, L. Fatal Multiple Fat Embolism in a Patient Given Salvarsan. *Am J Syph & Neurol* **14** 43 (Jan.) 1930.

6 Brittingham, J. W., and Phinzy, T. Hemorrhagic Encephalitis After Neoarsphenamine. *J A M A* **96** 2021 (June 13) 1931.

7 Thurmon, Francis M., and Tolman, Maurice. Acquired Hypersensitivity to the Arsenobenzol Radical of Bismarsen. *New England J Med* **209** 540 (Sept. 14) 1933.

# DERMATITIS PAPILLARIS CAPILLITII AND SYCOSIS VULGARIS WITH HYPOVITAMINOSIS

## REPORT OF A CASE

THOMAS B HALL, MD

KANSAS CITY, MO

The occurrence of pathologic cutaneous changes in cases of hypovitaminosis has been reported recently by Scheer and Keil,<sup>1</sup> Sweitzer, Loewenthal<sup>2</sup> and others. Follicular hyperkeratotic papules, follicular pustules, acneiform eruptions, intracutaneous hemorrhages and xerosis have been described as occurring in cases of hypovitaminosis.

That such dermatoses as sycosis vulgaris and dermatitis papillaris capilliti may be produced by hypovitaminosis is strongly suggested by the following case.

## REPORT OF CASE

*History*—C H, a Negro aged 39, was first seen at the Kansas City General Hospital no 2 on July 2, 1935. He had been an inmate of a state prison for the past nine years, obtaining his release in May 1935. While in prison he was rather frequently subjected to discipline by being placed on a restricted diet. At one time he was placed on a diet of bread and water as a corrective measure. The usual prison diet was said by the patient to be deficient in butter, milk, eggs, fresh fruits and vegetables. Since his release from the prison he had obtained an irregular and inadequate diet.

The onset of the cutaneous disease was in 1932, while the patient was an inmate of the prison. At that time he noticed a few hard lumps the size of a pea on the front of his chest. Occasionally one of these lumps became filled with pus. Shortly after the onset, similar lesions appeared on the entire trunk, the back of the neck and the extremities. A few of the lesions became full of pus and "seemed to spread" to other areas. While the patient had never been entirely free from the eruption, at irregular intervals he noticed a marked improvement. Pruritus had been a persistent and annoying symptom.

During the past year the eruption had become severe on the back of the neck. "Many hard lumps" formed, some of which contained pus. Within the past year the patient had also noticed a severe involvement of the hairs of the face and the pubic area. Pus formed around many of the hairs, and there was a considerable loss of hair in the affected pubic area.

Many lotions and salves were applied while the patient was in the hospital, with no benefit. The application of ammoniated mercury ointment seemed to have no effect.

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1 Scheer M., and Keil, Harry. Follicular Lesions in Vitamin A and C Deficiencies, Arch Dermat & Syph **30** 177 (Aug) 1934.

2 Sweitzer, S. E. Minnesota Med **16** 670 (Nov) 1933.

3 Loewenthal L. J. A. A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency, Arch Dermat & Syph **28** 700 (Nov) 1933.

Although there was no history or serologic or clinical evidence of syphilis, the patient had recently been given several injections of neoarsphenamine. This treatment caused no improvement but resulted in an increase in the pruritus and in the dryness of the skin.

Because of the history of deficiency of vitamins in the diet and the nature of the cutaneous eruption, the patient was carefully questioned as to visual disturbances. During the past few years reading by artificial illumination had become so difficult that he was forced to give it up. The letters seemed to blur and fade out. While working on the prison farm, he noticed that he was unable to see as clearly in twilight as the other prisoners. Distant objects seemed to fade out, and unless he was familiar with the ground he became lost. For this reason, during twilight and at night he tried, as much as possible, to stay with the prisoners whose eyesight was better than his.

*Examination*—The general physical examination gave essentially negative results.

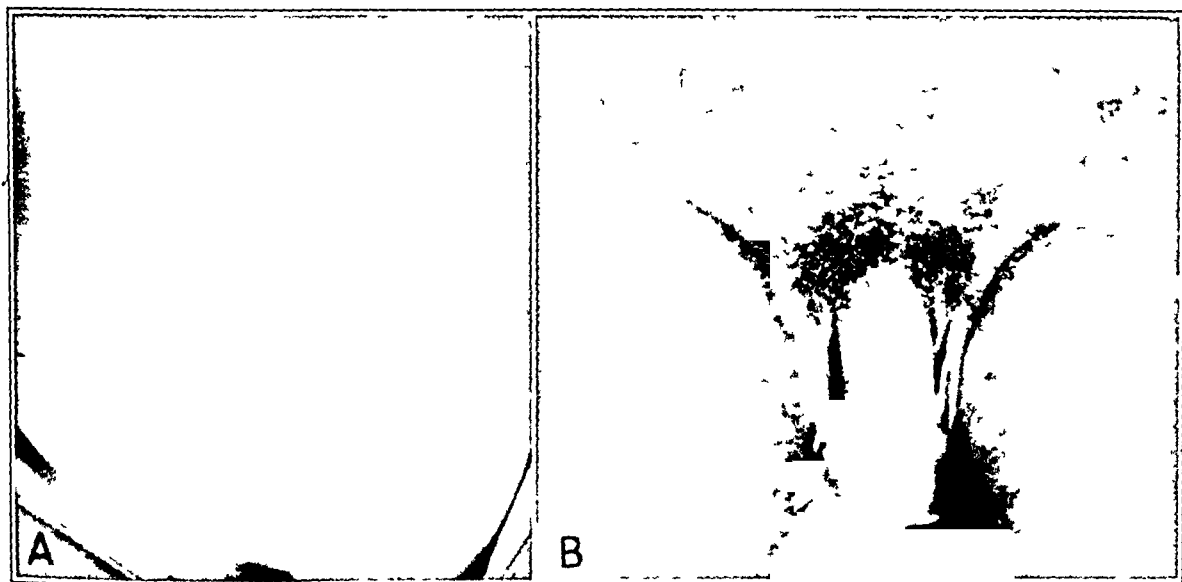


Fig 1—*A* is a posterior view of the trunk, with diffuse keratotic folliculitis and occasional follicular keratotic papules the size of a split pea. *B* shows pustular folliculitis of the hairy pubic area.

The skin, except that of the face, was xerotic. The normal oily luster of the Negro skin was absent, except on the face. There was a mild branny, scaly desquamation of the skin of the inner and outer surfaces of the thighs, outer surfaces of the arms and flexures of the elbows.

There was a generalized follicular papular hyperkeratosis of the skin of the trunk and the extremities. The keratotic follicular papules were as a rule, the size of a pinhead, noninflammatory and nonsuppurative. There were, here and there, much larger but similar isolated papules the size of a split pea. Occasionally one of these larger papules showed signs of an inflammatory reaction and pustulation.

In the pubic area the most prominent feature was wide-spread pustular folliculitis. Here and there were small hyperkeratotic follicular papules. There was loss of hair in irregular areas.



On the face the bearded region was markedly affected. In this area were numerous thick-set follicular papulopustules. From many of these lesions a bead of pus could be expressed by pressure. The inflammatory reaction and pustulation were marked in comparison with the occasional pustule and inflammatory papule on the trunk and the extremities. The inflammatory follicular pustules of the bearded area could not be differentiated from those occurring in cases of so-called coccogenous syccosis barbae. On the forehead were numerous noninflammatory follicular keratotic papules the size of a pinhead.

On the back of the neck the eruption was identical with that of dermatitis papillaris capillitii. In the lower, hairy portion of the posterior area of the neck were numerous large conglomerate follicular papulopustules. This area of the neck had a boggy feel, and on pressure pus exuded from many of the follicular openings. In some areas the pustules had undergone healing by cicatrization. On

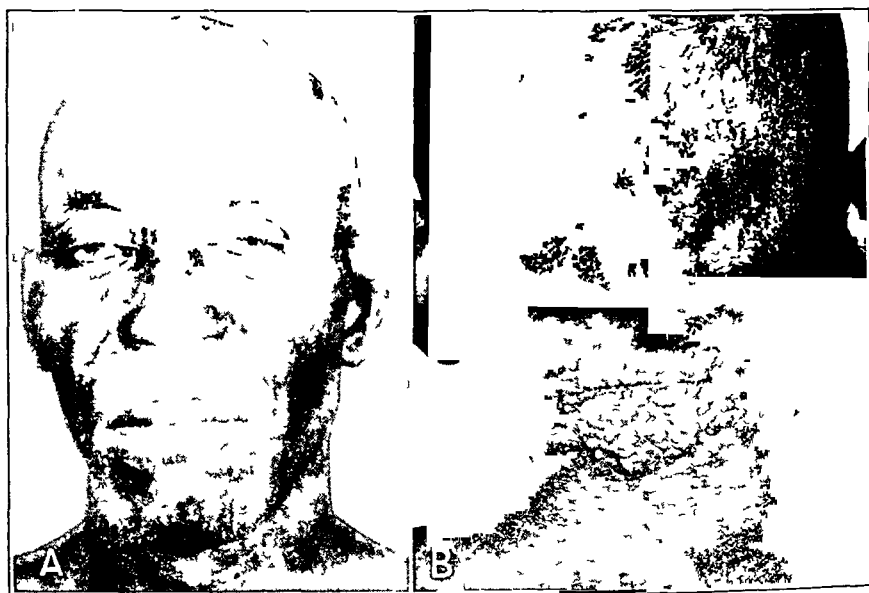


Fig. 2—*A* shows follicular pustular lesions of the bearded region, and *B*, the back of the neck, with dermatitis papillaris capillitii.

the posterior area of the scalp, above the extensively affected area, were a few scattered follicular papulopustules.

*Treatment*—From the clinical appearance of the cutaneous lesions and the history of the patient, it was thought probable that hypovitaminosis was responsible for the cutaneous changes. The history of night blindness indicated that a deficiency of vitamin A must be present. To compensate for this deficiency, cod liver oil was prescribed in doses of 1 tablespoonful three times a day.

After the patient had taken cod liver oil for two weeks, the skin was examined. Marked regression in the activity of the cutaneous lesions had apparently taken place. The large inflammatory papulopustules on the face and elsewhere had regressed to approximately half the size they were at the time of the first examination. Fewer of the papules were undergoing pustulation, and there seemed to be no new papules or pustules developing. The patient reported a considerable decrease in the annoying pruritus.

Two weeks later (four weeks after cod liver oil was prescribed) the patient was examined. At this time it was apparent that further regression in the size and activity of the lesions had taken place. In the area affected by the dermatitis papillaris capillitii only one superficial pustule was present. In comparison with the great number of pustules present on the first examination, the improvement was striking.

#### COMMENT

The occurrence of certain cutaneous changes as a result of hypovitaminosis seems to be well established.

That hypovitaminosis may also produce cutaneous changes hitherto regarded as being purely of bacterial origin, is strongly suggested in this case.

That the follicular involvement caused by hypovitaminosis may undergo suppuration and produce the identical picture of dermatitis papillaris capillitii and sycosis vulgaris is probable. The fact that in my case the involvement of the bearded area, the back of the neck and the pubic area was preceded and accompanied by the characteristic follicular hyperkeratosis of hypovitaminosis (deficiency of vitamin A and possibly of vitamin D) makes it probable that the two conditions were of the same genesis.

The occurrence of night blindness indicated definitely a deficiency of vitamin A. The favorable therapeutic effect of cod liver oil on the sycosis and dermatitis papillaris capillitii, while indicative of vitamin deficiency as an important factor in the causation, does not prove that a lack of vitamin A was solely responsible, since it is well known that cod liver oil contains both vitamin A and vitamin D.

Although in none of the cases reported by Loewenthal<sup>3</sup> was sycosis or dermatitis papillaris capillitii present, in other respects the eruption in my case closely simulated that in Loewenthal's case. Loewenthal attributed the cutaneous changes in his cases solely to a deficiency of vitamin A. In this connection it is interesting to call attention to the favorable response, which has long been noted, that the empirical use of cod liver oil sometimes gives in cases of sycosis vulgaris.

In a discussion of the systemic treatment of sycosis vulgaris Stelwagon<sup>4</sup> stated: "In some cases there is an underlying constitutional debility which, unless corrected, seems to add to the obstinacy of the disease. In such cases cod liver oil is an admirable remedy, the administration of which not infrequently quite perceptibly aids in obtaining a result from local measures."

Likewise long before it was recognized that night blindness was caused by deficiency of vitamin A cod liver oil was advocated in its treatment.

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<sup>4</sup> Stelwagon H. W. *Diseases of the Skin*, ed. 8 Philadelphia: W. B. Saunders Company, 1918.

Schmidt-Rimpler<sup>5</sup> stated "Cod liver oil has been recommended as a specific remedy" Wise and Sulzberger stated "The study of the effect of vitamins on the skin is but beginning There may be many forms of relative hypovitaminosis leading to pictures not now recognized as connected with vitamin deficiency"

Recent discoveries make it highly desirable that a critical evaluation be attempted to estimate the rôle of the vitamins in the production of the follicular dermatoses

#### SUMMARY

A case of sycosis vulgaris and dermatitis papillaris capillitii has been reported in which hypovitaminosis apparently was the causative factor

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<sup>5</sup> Schmidt-Rimpler, H Ophthalmology and Ophthalmoscopy, New York, William Wood & Company, 1889

## Minor Notes

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### TREATMENT OF RHINOPHYMA BY ELECTRO-DESICCATION

JOSEPH V KLAUDER, M D, PHILADELPHIA

I regard the following method of treating rhinophyma as superior to that of surgical ablation. Local anesthesia is employed. The electrodesiccating needle (unipolar method) is inserted into the rhinophyma. The current is turned on sufficiently long to allow the area treated to become quite blanched. This blanched area is trimmed away with a scalpel down to undesiccated tissue, which bleeds



*A*, rhinophyma before destruction, *B*, result of treatment by electrodesiccation and paring

freely when cut. The blanched area bleeds little if at all and cuts with a resistance comparable to that of a raw potato. If necessary the needle is inserted into the same area and more tissue is desiccated, which in turn is cut away. This procedure is repeated at different areas until the entire rhinophyma is destroyed. Judgment must be exercised in order not to destroy too much or too little and to maintain the normal contour of the nose.

With this method of treating rhinophyma the operative field is almost bloodless and destruction can be better controlled. These advantages favor a good cosmetic result. I do not believe that the unipolar method of electrodesiccation employing a cutting current is a more desirable method since there is less control of destruction with the cutting current.

The illustration shows a patient whose rhinophyma was destroyed by the aforementioned method of treatment: a combination of electrodesiccation and paring.

ALLERGIC CUTANEOUS ERUPTIONS AFTER HIGH  
VOLTAGE ROENTGEN THERAPY

V PARDO-CASTILLO, M D, HAVANA, CUBA

I wish to report on four cases of disseminate eruptions of the skin occurring after high voltage roentgen therapy. All four patients were white men who had received several doses of high voltage roentgen therapy for a malignant tumor. In two cases the tumor was located in the mouth, with metastases to the glands of the neck, in one, in the testicle, with metastases to the glands of the groin, and in one, in the stomach, the roentgen therapy being applied to the epigastric and dorsal regions, after gastrectomy.

The patients had general symptoms consisting of malaise, nausea and vomiting and slight elevations of temperature. Several days later, two of the patients showed morbilliform eruptions, one showed disseminate areas of erythema, resembling erythema multiforme, and one had large, edematous papules on the trunk, neck and extremities, resembling the lesions of chickenpox in their first stage. Subjective sensations were absent, except for a slight pruritus of the morbilliform types.

Artz and Fuhs<sup>1</sup> stated that "certain general reactions are at times observed soon after the treatment, even of a circumscribed area of the skin. For instance, in many forms of tuberculosis, leukemia, etc., a rapidly fading scarlatiniform or small papular rash may develop with pyrexial attacks. This reaction is supposed to be due to an intoxication caused by the absorption of the products of cellular degeneration (x-ray toxin). In so far as any treatment appears necessary, rest in bed with the application of a powder is indicated."

Moore<sup>2</sup> reported a case of widespread angioneurotic edema in a woman receiving postoperative irradiation for cancer of the breast.

In all my cases the rash disappeared spontaneously in a few days, except in the third case, in which the erythema multiforme-like eruption persisted for nearly three weeks and faded gradually.

These patients were seen in a period of three years, and an attempt is being made to follow up all persons subjected to high voltage irradiation in order to determine the frequency of these reactions.

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1 Artz, L., and Fuhs, H. *Rontgen Rays in Dermatology*, translated by C. Kevin O'Malley, New York, William Wood & Company, 1927, p. 75.

2 Moore, quoted by Bray, G. W. *Recent Advances in Allergy*, Philadelphia, P. Blakiston's Son & Co., 1934, p. 429.

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

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THE CHEMOTHERAPY OF CANCER 1 LEAD J A BARGEN, BAYARD T HORTON and ARNOLD E OSTLERBERG, *Am J Cancer* **23** 762 (April) 1935

These investigators believe that systemic treatment of cancer with lead offers an additional hope in control of cancer when it is used in conjunction with radiotherapy and surgery. The intravenous injection of lead to the point of producing intoxication apparently affects body metabolism to the extent of suppressing neoplastic growth.

METASTASIS OF A SQUAMOUS CELL CARCINOMA FROM THE WRIST TO THE AXILLA WITHOUT DEMONSTRABLE INTERVENING GROWTH ESMOND R LONG, *Am J Cancer* **23** 797 (April) 1935

Serial sections of an amputated upper extremity failed to show evidence of lymphatic extension from a primary lesion of the wrist to an axillary metastasis. It was therefore assumed that the metastasis was the consequence of lymphatic embolism.

ECTODERMAL TUMORS OF THE SKIN CHARLES F GRSCHICKER and HENRY P KOEHNER, *Am J Cancer* **23** 804 (April) 1935

The authors discuss both benign and malignant cutaneous lesions and group the malignant lesions under the headings of epidermal cancer and appendage cancer. The former are subdivided into keratinizing and nonkeratinizing and the latter into nonmetastasizing and metastasizing lesions. Basal cell epitheliomas are classified as nonmetastasizing appendage cancers and squamous cell epitheliomas as acanthomas or keratinizing epidermal cancers. The effect of actinic rays and carcinogenic substances in the development of precancerous and cancerous lesions is discussed. The classification of Broders and MacCarty is adopted for the differentiation of epidermal cancer.

HISTOGENESIS OF LYMPHOSARCOMATOSIS J C EHRLICH and I E GIBBER, *Am J Cancer* **24** 1 (May) 1935

Lymphosarcomatosis is described as a blastomatous disease arising in, and confined to, lymphoid tissue usually beginning in the lymph nodes and extending progressively via the lymphatics and the blood stream or occurring autochthonously in scattered centers of lymphatic tissue. Three types are discussed, the reticular, intermediate and lymphocytic. A morphologic comparison is drawn between the cells of these groups of lymphosarcoma and the immature, intermediate and mature cells resulting from the normal differentiation of the cytoplasmic reticulum.

NEOPLASM STUDIES 1 CELLS OF MELANOMA IN TISSUE CULTURE C G GRAND, ROBERT CHAMBERS and GLADYS CAMERON, *Am J Cancer* **24** 36 (May) 1935

The authors have successfully grown human as well as mouse melanomas in tissue culture. No epithelial outgrowth was obtained and three types of cells were recognized in the outgrowth—macrophages, fibrocytes and melanoblasts. The melanoblasts were dendritic cells. The melanin is apparently produced by the melanoblasts and ingested by the macrophages.

TELE-CURIE-THERAPY B F SCHREINER, M C REINHARD and W H WEHR,  
Am J Cancer **24** 386 (June) 1935

A description and discussion of the treatment of malignant tumors by gamma rays of radium applied at a distance from the skin are given. From 1 to 5 Gm of radium was applied in packs at from 5 to 10 cm distance, with platinum, copper and aluminum filtration.

THE PERIPHERAL MANIFESTATIONS OF THE SPECIFIC NERVE SHEATH TUMORS (NEURILEMOMA) ARTHUR P STOUT, Am J Cancer **24** 751 (Aug) 1935

The neurilemmoma, or nerve sheath tumor, is not an uncommon lesion, but it is usually mistaken for a fibroma, lipoma, ganglion, cyst or myxoma. The lesion is usually solitary, asymptomatic, sharply defined and subcutaneous, and frequently it is situated on the extremities, face and scalp.

FOERSTER, Milwaukee

THE INFECTIVITY OF *TREPONEMA PALLIDUM* IN EXCISED SYPHILITIC TISSUE P D ROSAHN, Am J Hyg **22** 283, 1935

Under ether anesthesia, rabbits with active syphilitic orchitis were castrated and the syphilitic tissue was stored at refrigerator temperature. At intervals varying from twenty-four hours to forty-two days, portions of the refrigerated syphilomas were ground up with saline solution and inoculated into test rabbits intratesticularly. Positive infections as determined by the clinical development of syphilitic lesions or by successful subinoculations of excised lymph nodes were obtained with syphilitic material which had been stored in the refrigerator for twenty-four hours, forty-eight hours, ninety-six hours and seven days. Negative results were obtained with material stored for fourteen, twenty-three and forty-two days. The infections varied with the age of the material from a typical disease to one of more than usual severity and finally to an asymptomatic infection which could be demonstrated with certainty only by subinoculation. It is suggested that in certain instances of human syphilis in which there is no history of a primary lesion the infection may have been initiated by attenuated spirochetes and that occasionally contaminated material, especially fomites from syphilitic patients, may be the source of attenuated spirochetes. *Spirochaeta pallida* in autopsy material which has been refrigerated for as long as seven days should be regarded as infectious.

FROM THE AUTHOR'S SUMMARY [ARCH PATH]

THE RELATION OF EXPERIMENTAL SKIN INFECTION TO CARBOHYDRATE METABOLISM THE EFFECT OF HYPERTONIC GLUCOSE AND SODIUM CHLORIDE SOLUTIONS INJECTED INTRAPERITONEALLY D M PILLSBURY and G V KULCHER, Am J M Sc **190** 169 (Aug) 1935

Pillsbury and Kulcher, using rabbits whose skin had been experimentally infected with staphylococci, injected parenterally 7.5 Gm of dextrose at intervals of twelve hours during a six day period. No effect was observed on the cutaneous infection with this dose.

Increasing the dose of dextrose to 15 Gm per kilogram in twenty-four hours resulted in a marked increase in the extent of the cutaneous infection.

Similar results were obtained by using solution of sodium chloride in similar amounts. These results indicate that a specific effect of dextrose as such was not the chief factor in producing the effects noted.

LYMPHOPATHIA VENEREUM (LYMPHOGRANULOMA INGUINALIS) AND ITS RELATION TO RECTAL STRICTURE J B VANDER VEER, F E CORMIA and J C ULLERY, Am J M Sc **190** 178 (Aug) 1935

Vander Veer, Cormia and Ullery briefly review the literature and symptomatology of lymphopathia venereum and analyze forty-seven cases of their own.

series In their series twenty-one patients presented rectal stricture, the remainder had inguinal adenopathy The authors found this syndrome more frequently in Negroes than in white persons, and they recommend that the Frei test be read after the fourth day Patients having an obscure inguinal adenopathy or rectal stricture should be subjected to a Frei test As an elimination measure the use of the Frei test is also advised in cases of obscure pelvic infections, perirectal abscess and fistulas in ano

HEREDITARY ONYCHIAL DYSPLASIA M E HOBBS, *Am J M Sc* **190** 200 (Aug) 1935

Hobbs reports the case of a patient presenting onychial dysplasia of the hereditary type and discusses the problem of the associated social aspects It is suggested that "the defects observed are due to the differential effects of one gene (D), acting during the process of development of the three primary body layers, its action ceasing on full development of the various parts"

FAMILIAL PURPURA REPORT OF TWO CASES F R BAILY and K R McALPIN, *Am J M Sc* **190** 263 (Aug) 1935

Baily and McAlpin report the cases of two brothers, Negroes, who presented a hemorrhagic diathesis with prolonged bleeding time, normal clotting time and a normal platelet count This condition is usually manifested in infancy or childhood, but the prognosis is good if the child reaches the age of 15 The name "constitutional thrombopathy" has recently been suggested for this condition

THE IMMUNOLOGICAL SPECIFICITY OF STAPHYLOCOCCI I THE OCCURRENCE OF SEROLOGICAL TYPES L A JULIANELLE and C W WIEGHARD, *J Exper Med* **62** 11 (July) 1935

From their attempts to classify staphylococci into serologically distinct types, Julianelle and Wieghard drew the following conclusions The existence of at least two immunologically distinct types was demonstrated by precipitation methods, one type, A, being composed of apparently virulent strains and the other type, B, containing the avirulent strains

Intravenous methods of immunization were found to stimulate formation of agglutinin, but formation of precipitin was stimulated in only about 25 per cent of the rabbits used in the experiment Formation of agglutinin is also stimulated by intracutaneous injections of dead staphylococci or of living organisms, but the formation of type-specific precipitins is not stimulated in that manner

THE IMMUNOLOGICAL SPECIFICITY OF STAPHYLOCOCCI II THE CHEMICAL NATURE OF THE SOLUBLE SPECIFIC SUBSTANCES C W WIEGHARD and L A JULIANELLE, *J Exper Med* **62** 23 (July) 1935

Two carbohydrates, immunologically and chemically distinct, were extracted from different strains of *Staphylococcus*, the chemical differences being manifested principally in optical rotation and in the simple sugars resulting from hydrolytic cleavage

Increasing hydrolysis dissipates the immunologic specificity of both polysaccharides

THE IMMUNOLOGICAL SPECIFICITY OF STAPHYLOCOCCI III THE INTERRELATIONSHIPS OF CELL CONSTITUENTS L A JULIANELLE and C W WIEGHARD *J Exper Med* **62** 31 (July) 1935

The conclusions drawn from the work of Julianelle and Wieghard indicate that the carbohydrates derived from *Staphylococcus* are type-specific although they fail to induce formation of antibodies in rabbits



of 2 cc every fourth day in courses of twenty injections. In the discussion which followed the presentation it was stated that reactions of intolerance to the drug have been known to occur.

**A CASE OF SYPHILITIC REINFECTION** J. GATE and P. CUIILLERET, *Bull Soc franç de dermat et syph* **41** 844 (June) 1934

What appears to be an authentic case of syphilitic reinfection is reported. The patient first presented a chancre and had a negative Wassermann reaction. Treatment was begun in this preserologic phase, neoarsphenamine and a bismuth preparation being administered for four years, and the serologic reactions remained negative throughout that period. Suddenly after exposure a penile lesion, clinically typical of chancre, developed, and although the Wassermann reaction of the blood was negative, spirochetes were demonstrated by dark-field examination.

**ACTION OF GOLD SALTS ON GENERAL PARALYSIS** A. SEZARY and A. BABBE, *Bull Soc franç de dermat et syph* **41** 866 (June) 1934

Nine patients with dementia paralytica were treated with gold sodium thio-sulfate, and while both the clinical and the serologic results were fairly good they were not superior to those obtained with acetarsone or malaria therapy.

**HEMORRHAGIC PANCREATITIS IN THE COURSE OF TREATMENT WITH ARSPHENAMINE** M. MILIAN, *Bull Soc franç de dermat et syph* **41** 914 (June) 1934

In a patient who had received antisyphilitic treatment for four years there developed a typical acute nitritoid crisis while an injection of arsphenamine was being administered. He was at once admitted to the hospital where he remained for six days, with the symptoms lumbar pain, diarrhea, scanty urine, intense thirst and incessant hiccups. The patient died, and autopsy revealed the presence of a hemorrhagic pancreatitis. Milian thinks that probably a syphilitic lesion of the pancreas was reactivated by the drug.

**DUHRING'S DISEASE SUPERVENING IN THE COURSE OF TREATMENT WITH GOLD SALTS** A. SEZARY and M. BOLGERT, *Bull Soc franç de dermat et syph* **41** 927 (June) 1934

In a woman aged 47 who was receiving treatment with gold salts for rheumatism, dermatitis herpetiformis developed. The authors interpret this as suggesting an allergic or biotropic origin for that disease and adding another condition to the long list of cutaneous complications of therapy with gold salts.

**HEREDITARY AND FAMILIAL PALMAR AND PLANTAR KERATODERMA** G. BASCH, ABRAHAM and F. SIGUIER, *Bull Soc franç de dermat et syph* **41** 945 (June) 1934

A mother and daughter had keratoderma of the palms and soles, and the mother's grandfather, her father, a sister and a brother were similarly afflicted. The mother's basal metabolic rate was + 18 per cent, that of the daughter was + 10 per cent, the authors regard this as possible evidence that thyroid dysfunction is the cause of this disease.

**SECONDARY SYPHILIS AND ASSOCIATED DIPHThERIA** M. J. MAX, *Bull Soc franç de dermat et syph* **41** 984 (June) 1934

A patient with proved secondary syphilis, who showed fever and marked symptoms of involvement of the throat, immediately received intensive treatment, and when his condition grew worse it was discovered that he had an associated diphtheria. The latter promptly responded to treatment with serum. When the patient recovered the Wassermann reaction was still 4 plus, and antisyphilitic therapy was resumed.

THREE CASES OF POLYMORPHOUS ERYTHEMA IRIS RAPIDLY DISAPPEARING AFTER A POSITIVE REACTION TO INTRADERMALLY INJECTED TUBERCULIN GOUGEROT and DLGOS, Bull Soc franç de dermat et syph **41** 1523 (July) 1934

The frequent occurrence of a strongly positive tuberculin reaction in patients with erythema multiforme is well known, but a favorable influence exerted on this disease by intradermal injections of tuberculin is a new phenomenon observed by Gougerot and Degos in three cases. They suggest that this method of treatment may be worth trying in cases of resistant and recurring polymorphic erythema.

PRICKLE CELL EPITHELIOMA AT THE BASE OF THE TONGUE IN A TWENTY-THREE YEAR OLD MAN WITH CONGENITAL SYPHILIS MILLIAN and DELAMARF, Bull Soc franç de dermat et syph **41** 1541 (July) 1934

An ulcer, measuring 3 by 2 cm, located on the posterior portion of the tongue of a patient with congenital syphilis, was proved by biopsy to be a prickle cell epithelioma. This is regarded as added evidence of the cancerogenic role of syphilis.

INTRAVENOUS ADMINISTRATION OF CHARCOAL IN DERMATOLOGIC THERAPEUTICS A. TOURAINE and B. MENETREL, Bull Soc franç de dermat et syph **41** 1580 (July) 1934

This article is a report on the results of treatment of twenty-five patients with various cutaneous conditions by means of intravenous injections of animal charcoal.

The following method was used. A finely pulverized suspension of animal charcoal (20 per cent) in physiologic serum was employed. The habitual dose, given daily, was from 3 to 4 cc, although it was found that 6 or 7 cc could be tolerated without ill effect. The number of injections ranged from two or three to six or eight and even ten. All other general and local treatment was suspended while this test was made.

The plunger of the syringe was oiled with liquid petrolatum to avoid wedging, and care was taken to avoid tattooing of the skin at the site of puncture.

No explanation regarding the mode of action is offered other than the following statement: "the clinical results seem to show clearly the existence of an anti-infectious action."

The injections were tolerated remarkably well, there being no instance of local or general reaction or of any of the phenomena of shock.

The results were as follows: 1. Rapid cure was obtained in the acute microbic infections, such as erysipelas, multiple abscesses, furuncles, impetigo and impetiginous eczemas. 2. In the more chronic conditions, such as psoriasis and chronic suppurations, the action was slower but favorable. 3. There was rapid amelioration of an acute attack of dermatitis herpetiformis, and remarkable retrocession of an exanthematic lupus erythematosus occurred.

GANDY, Houston, Texas

THERAPEUTIC EFFECTS OF NONCHLORIDE DIETS OF NURSING MOTHERS ON THE CUTANEOUS EXUDATIVE MANIFESTATIONS IN NURSING VITALIANO SACCO, *Pediatrics* **42** 1432 (Dec) 1934

Sacco presents a brief review of the known concepts pertaining to the pathogenetic mechanism of exudative diatheses and gives the result of his experience relative to the therapeutic effects of a nonchloride dietetic regimen in the nursing mother on cutaneous exudative manifestations in the infant.

In his case the reduction of sodium chloride in the mother's diet led to a disappearance of the cutaneous exudative lesions in the nursing

PURULENT COMPLICATIONS IN ERYSIPELAS OF THE NEW-BORN N CARRARA,  
*Pediatrics* **43** 184 (Feb) 1935

A case of erysipelas in a 12 day old infant is reported in which complicating purulent arthritis of the knee was associated with a favorable influence on the erysipelas

SIGNORELLI, New Orleans [AM J DIS CHILD]

INFECTIOUS ERYTHEMA (FIFTH DISEASE) A ROMEO LOZANO, *Pediatrics españ*  
**23** 307 (Sept) 1934

The author reports eleven cases of this disorder, the first series reported in the Spanish pediatric literature. The patients were observed during summer and winter months. The incubation period seemed to vary between six and seven days, but the author is under the impression that it may be even longer.

The eruption appears first about the nose and the eyelids. The face appears swollen, as though it had sustained a blow. The early redness of the rash changes to a bluish and violet-gray tinge. The eruption may also appear on the forehead and on the chin. *Simultaneously or a day or two later the eruption appears on the extremities and may involve the palmar and plantar surfaces.* For the most part, it consists of small red spots, slightly raised and closely resembling urticarial eruptions. At times they become confluent and may assume an annular form. The type is particularly liable to occur if the eruption involves the trunk. No desquamation takes place. A normal leukocyte count or slight leukopenia is observed. Nephritis and moderate forms of arthritis may be complications but were not observed by the author in his series of cases. No treatment is required. The prognosis is uniformly good.

SCHIUTZ, Chicago [AM J DIS CHILD]

CUTANEOUS ERUPTION IN CASES OF APHTHOUS STOMATITIS R MAYER, *Arch f Kinderh* **103** 78, 1934

Two cases of aphthous stomatitis in which lesions occurred on the skin of the face and body as well as on the mucous membrane of the mouth are reported. The author believes that aphthous stomatitis is an exanthematous disease and that the lesions are indicative of a hematogenous effect just as the rash of measles and scarlet fever.

APHTHOUS STOMATITIS P VON GARA and W HERTZ, *Arch f Kinderh* **103** 204, 1934

In order to prove the contagious character of aphthous stomatitis the virus was inoculated into guinea-pigs. Typical vesicles developed, and immunity against repeated inoculation was also observed. The virus of herpes simplex when inoculated into guinea-pigs also produced positive reactions. Guinea-pigs inoculated with virus of aphthous stomatitis showed partial immunity to subsequent inoculation with herpes virus. Conversely, the animals inoculated with herpes virus showed no reaction when subsequently inoculated with virus of aphthous stomatitis. The authors conclude that the virus of herpes simplex and that of aphthous stomatitis are similar.

ERYTHEMA NODOSUM AND SCARLET FEVER DENES VON MORITZ, *Arch f Kinderh* **103** 227, 1934

The author reports two cases in which erythema nodosum occurred during convalescence from scarlet fever. In both cases no roentgen evidence of tuberculosis could be demonstrated, and the Mantoux tuberculin reaction was repeatedly negative. The author believes that although most instances of erythema nodosum occur in tuberculous patients, there is occasionally a case of erythema nodosum due to allergy to the streptococcus, such as occurred in these two patients.

LEMASTER, Evanston, Ill [AM J DIS CHILD]

PSORIASIS AND THE BLOOD PICTURE ILSE STUTZIL-GERNECK, *Dermat Wehnschr* **100** 613 (June 1), 645 (June 8) 1935

From a study of the blood picture in 140 cases of psoriasis observed during the past ten years the author draws the following conclusions 1 There is usually an increase in the lymphocyte count 2 The lymphocytosis was present in 69.28 per cent of the cases before, and in 78.56 per cent after, treatment 3 An eosinophilia was present in four cases before, and in one after, treatment 4 Transitional forms were present in normal numbers 5 There was no relationship between the blood count and the course of the disease or the type of treatment The extent of the condition had no influence on the blood count

HYGIOTHERAPY AND HIGH ALTITUDE IN THE TREATMENT OF LUPUS A ROLLIER, *Dermat Ztschr* **71** 237 (July) 1935

Rollier discusses the benefit of generalized exposure to the rays of the sun at high altitudes in the treatment of lupus vulgaris He describes the gradual increase of the exposure and shows several photographs of patients before and after treatment He refers to the beneficial psychic influence of satisfactory institutional care in pleasant surroundings

RESULTS OF A DRY BLOOD TEST IN SYPHILIS S LEIPNER, *Dermat Ztschr* **71** 247 (July) 1935

A drop of blood was stirred on a microscope slide and allowed to dry The dried blood was then dissolved in a 3.5 per cent solution of sodium chloride, and 0.03 cm of diluted Memmick's clearing reaction extract warmed to from 55 to 56 C was added and the slide shaken for three minutes The reaction was noted under the microscope in from five to ten minutes and again in half an hour In negative reactions there was a homogeneous granular appearance, the positive reaction was evidenced by various grades of clumping In one hundred and fifty tests the reaction was found to closely parallel the results of other standard tests

DERMATOMYCOSIS CAUSED BY UNUSUAL STRAINS OF PARASITES EMANUEL WEISZ, *Dermat Ztschr* **72** 1 (Aug) 1935

Weisz briefly cites instances reported in the literature of cutaneous disorders caused by various unusual organisms many of which are usually considered non-pathogenic They include conditions caused by *Aspergillus*, *Penicillium* and other molds

TAUSSIG, San Francisco

ETIOLOGY OF PELLAGRA L A TSCHIRKES, *Vrachi delo* **17** 691 1934

The present status of the question of the etiology of pellagra is given on the basis of a review of literature as well as of personal experimental and clinical observations

Pellagra develops in consequence of prolonged homogenous feeding when food is lacking in the antipellagic substance (vitamin P) A series of facts speak against the identification of vitamin B with the antipellagic factor

Although the main pellagra-producing factor is the lack of the antipellagic substance in the food, other factors are also involved in the development of pellagra but their nature is not yet known There are some grounds for presuming that an inadequate amount of proteins may be considered one of these factors

The question as to whether the conditions obtained up to the present time in experimental animals (rats, mice, dogs and monkeys) are identical with human pellagra remains unsolved

Although the question of the etiology of pellagra has not as yet been definitely settled the known therapeutic and prophylactic measures as shown by laboratory and clinical experimentation, are effective

BODER, Los Angeles [AM J DIS CHILD]

**ULCUS VULVAE SIMPLEX CHRONICUM** RAFAEL JACOBSEN and V PARDO-CASTELLO,  
Acta dermat-venereol **16** 133 (July) 1935

Four cases of chronic ulcerations of the vulva are reported. The condition was characterized by the location of the ulcers on the fourchet or on the introitus of the vagina, by the presence of the lesions in inveterate prostitutes and by the hard leathery edges. The ulcers were indolent, the patients ignoring their presence and in some cases being entirely unaware of their existence. No etiologic agent was found, and treatment was unsuccessful. The differential diagnosis is discussed. The literature on esthiomene is reviewed.

**THE SENSITIVITY OF THE SKIN TO LIGHT IN XERODERMA PIGMENTOSUM** B B HEFT,  
Acta dermat-venereol **16** 146 (July) 1935

The literature on this subject is reviewed. A case is described in which the patient, a man aged 20, showed a diminished sensibility to ultraviolet rays and all chemicals in the parts of the skin affected by xeroderma pigmentosum and a perfectly normal sensibility to these irritants in the healthy parts of the skin. The sensibility of this patient to roentgen rays was normal. The decreased sensitivity of the affected part of the skin to ultraviolet rays and chemicals in this patient may be explained by a desensitization or by an increase in the defense ability of the involved skin.

**THE SO-CALLED NORMAL SALT RETENTION IN SKIN DISEASES** J R PRAKKEN,  
Acta dermat-venereol **16** 156 (July) 1935

The amount of chloride in the urine is sometimes diminished in pemphigus and, to a lesser degree, also in other cutaneous diseases. This question was investigated by Prakken, who observed and studied the amount of chloride in ten cases. A moderate deficiency of chlorides in the urine was present in one case of dermatitis exfoliativa and in three cases of eczema. A marked deficiency of chlorides in the urine was found in two cases of pemphigus vulgaris during the stage of eruption of bullae. There was no retention of the chlorides in the body at that time. The author believes that this is proved by the fact that chlorides did not appear in more than normal quantities in the urine after the disappearance of the lesions. He thinks that the deficiency of the salt in the urine observed in some cutaneous diseases may be explained by the increased excretion through the skin.

**SOME REMARKS ABOUT THE MODERN TREATMENT OF SYPHILIS WITH BISMUTH**  
KAREL HUBSCHMANN, Acta dermat-venereol **16** 178 (July) 1935

The author is of the opinion that the introduction of bismuth therapy has made it possible to influence the course of syphilis by the continued presence of the drug in the body. He bases his assertion on skiascopic observations and examinations of the urine, which proved the presence of bismuth in the body two hundred days after the last injection of a preparation containing the drug. He also maintains that excretion of bismuth through the urine begins during the first twenty-four hours after the injection. Clinical observations have shown that a certain amount of bismuth was absorbed already during the first twenty-four hours after the injection influencing therapeutically the course of syphilis. The author agrees with others that sodium thiosulfate accelerates the excretion of heavy metals from the body. He cites a case in which this was proved not only by an increase in the quantity of bismuth found in the urine but also by roentgenograms.

ASTRACHAN New York

# Society Transactions

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## MINNESOTA DERMATOLOGICAL SOCIETY

D D TURNACLIFF, M D, *Secretary*

*April 12, 1935*

H E MICHELSON, M D, *Presiding*

DERMATITIS DUE TO POILEN Presented by DR H E MICHELSON, Minneapolis

P S, a man aged 75, states that for eight years he has suffered from a recurrent seasonal eruption which begins in June and lasts until frost occurs. The initial symptoms started on the face, they consisted of erythema and pruritus. Later there developed erythema, vesicles and edema which involved the entire body. The severity of these symptoms necessitates annual hospitalization. There is no eruption at present. The family history does not disclose a tendency to allergy. Patch tests gave positive results with the allergenic oils of pollen of timothy, pasture sage and plantain. Passive transfer tests gave negative results.

DERMATITIS DUE TO INHALANT DUST Presented by DR H E MICHELSON, Minneapolis

H J, a woman, aged 34, states that for eighteen months she had a pruritic eruption on the face and neck. The disorder later involved the hands, arms and body. The patient had a vasomotor rhinitis for several years, and this has become much worse since the eruption has been present. The severity of the rhinitis varies directly with the severity of the cutaneous condition. There is a family history of allergy. At present the eruption affects the face, neck, chest and arms. It consists of patches and plaques of erythema, papules, vesicles, crusts and fissures. Tests with an extract of autogenous house dust gave a 4 plus reaction. Patch tests with English lavender powder also gave a 4 plus reaction.

ATOPIC ECZEMA PROBABLY DUE TO INHALANT DUST Presented by DR SAMUEL E SWEITZER, Minneapolis

Mrs J, aged 25, complains of an eruption on the face, neck and arms which appeared when she was 6 months of age. The patient had no symptoms between the ages of 7 and 13 years. The last recurrence was antedated by the onset of menstruation. The patient has had bronchial asthma for the past few years, this is worse in the winter and generally precedes the exacerbation of the cutaneous eruption. She has been hospitalized several times, and each time hospitalization was followed by prompt remission of symptoms. There is a family history of allergic disease. At present the eruption involves the face, neck, chest and arms, it consists of papules, areas of lichenification, vesicles and crusts and is most marked on the sides of the neck and in the antecubital spaces. The skin gave positive reactions to a few foods and markedly positive reactions to autogenous house dust.

ATOPIC ECZEMA Presented by DR S E SWEITZER

D S, a boy aged 12 years, has had a pruritic eruption involving the face, arms and chest since infancy. This eruption increases in severity during the winter. During the past two years the patient has also had symptoms of vasomotor rhinitis. Hospitalization resulted in relief of symptoms. Physical examination

gave normal results except for the eruption, which involves the face, neck, arms and chest and consists of papules, lichenification and thickening of the skin. The eruption is most marked over the nape of the neck and antecubital spaces. There is no family history of allergic disease. Cutaneous tests gave essentially negative reactions except the test with autogenous house dust, which gave a 3 plus reaction.

#### DISCUSSION

PROF. FRANZ BLUMENTHAL, Ann Arbor, Mich. (by invitation). It seems interesting that atopic eczema is much more frequent in this country than in Berlin. One sees many cases in which atopic eczema is associated with dermatitis venenata, in these cases the patient is often sensitized to the preparations which have been used (tar, sulfonated bitumen, etc.). One of the patients presented exhibited a mixture of the two forms, atopic eczema and dermatitis venenata. If the dermatitis venenata is superimposed on an atopic eczema, it may be difficult to find out the true connection.

Concerning the therapeutic effect of desensitization, I have seen good results only in cases of atopic eczema, and even in such cases good results were not obtained regularly. In cases of dermatitis venenata I have not seen definite therapeutic effects. It is best to avoid contact with the irritant factor. One must not forget that treatment with tar and roentgen and ultraviolet irradiation all give good results, often the patient recovers and remains free from recurrence for a long time.

DR. ELMER RUSTEN, Minneapolis. The dermatitis due to pollen represents a seasonal eruption of external origin. Patch tests with allergenic oils of pollen of timothy, plantain and prairie sage gave positive results, these results agree with the history. Desensitization with these materials should be attempted.

The eruptions due to inhalant dust are atopic eczema in which other allergic manifestations correlate with the increase in cutaneous symptoms, one patient having bronchial asthma and the other vasomotor rhinitis. It is probable that these two patients have eruptions due to inhalants. Patch tests with house dust and other materials gave negative results, while scratch and intradermal tests with glycerinated extract produced large areas of cutaneous reaction. Subcutaneous injection of autogenous house dust will be used in treatment.

DR. R. J. BAILEY, Rochester, Minn. With the increasing use of the patch test the diagnosis of recurrent seasonal dermatitis of the contact type caused by the oils of ragweed and other plants has been greatly facilitated. However, at the Mayo Clinic attempts at desensitization by injection of a solution in oil of the fraction of the pollen soluble in fat solvents have so far proved unsuccessful in these cases.

I agree with Dr. Rusten that the eruptions due to inhalant dust are typical of atopic eczema.

PSYDOPLEADE OF BROCK. Presented by DR. H. E. MICHFISON, Minneapolis.

G. H., a man aged 32, states that eight years ago he noticed slight itching of the scalp associated with gradual loss of hair, without signs of inflammation.

There is an almost completely bald area measuring 5 cm. in diameter on the crown of the head. The involved area is smooth and shows no redness but presents atrophic scars.

#### DISCUSSION

PROF. FRANZ BLUMENTHAL, Ann Arbor, Mich. (by invitation). There are small spots and atrophic scars which may have started from folliculitis decalvans.

XANTHOMA WITH LIPEMIA. Presented by DR. H. G. IRVING, Minneapolis, and DR. D. D. TURNACIFF, Minneapolis.

This man aged 26, is 59 inches (149.86 cm.) tall. In February 1935 he weighed 165 pounds (74.9 Kg.), in April 1935 his weight had decreased to 140 pounds (63.5 Kg.). Apparently he is suffering from pituitary deficiency. Up to the age

of 9 years he was a small thin child, he had the usual diseases of childhood and severe influenza with pneumonia in 1918. Since then he has not been ill. He has maintained his weight at about 165 pounds for the past five years. Eighteen months ago he noticed the first cutaneous eruption on the dorsa of his hands. New lesions gradually developed on the extensor surface of the forearms on the upper portion of the arms, on the extensor surface of the knees and on the back. The last lesion to appear was one on the upper lip.

The lesions are nodules from the size of a pinhead to that of a pea with the characteristic color of xanthoma. A biopsy specimen was shown at the meeting of the society in February. At that time the blood serum was the color of cream. The results of chemical determinations on the blood serum in February and in April and the normal value are shown in the following tabulation (values per hundred cubic centimeters of blood serum).

	February	Normal Content	April
Total lipids	4,789.6 mg	570.820 mg	656.1 mg
Total fatty acids	3,879.6 mg	190.420 mg	428.1 mg
Total cholesterol	910.0 mg	100.230 mg	228.0 mg
Cholesterol esters	600.0 mg	40.70% of total	
Free cholesterol	310.0 mg	30.60% of total	
Ice thin	875.8 mg	175.330 mg	235.0 mg
Iodine absorbed	6,832.0 mg		
Iodine number	160.6	100.150	
Total protein	6.53 Gm	6.57.98 Gm	
Nonprotein nitrogen	37.2 mg	20.36 mg	

Since the patient was presented in February his diet has been restricted to 900 or 1,000 calories with a low intake of carbohydrates. The patient has followed that diet while doing his regular work and living at home. His weight has decreased from 165 to 140 pounds and the weekly examination has shown that there has been a diminution in the size of the lesions and that the newer lesions have disappeared.

The lipid content of the blood is now normal.

To rule out the possibility of the juvenile type of xanthomatosis roentgenograms of the skull and pelvic bones were made. They showed no abnormality.

The urine contained a trace of albumin but no casts. Sugar was present during the dextrose tolerance test, the results of which were as follows.

Sugar Content of the Blood	Mg per 100 Cc	Sugar Content of the Urine
During fasting	160	Negative
After ½ hour	255	4 plus
After 1 hour	315	
After 2 hours	237	
After 2½ hours	170	4 plus

The basal metabolic rate was — 12 per cent.

#### DISCUSSION

DR D. D. TURNACIFF, Minneapolis. There is another type of lipemia called the juvenile type of xanthomatosis, patients with that condition have lipemia and necrotic areas in the bones. That disorder is frequently associated with diabetes insipidus and other symptoms of pituitary disturbance.

In the past patients with that condition have been treated with roentgen radiation, and questionable results have been obtained but recently in Detroit one patient was treated by dietary regulations, as were Dr. Wile's patients and this one, and the clinical response was encouraging.

Patients with acromegaly have glycosuria and xanthoma superimposed on a background of pituitary disease and those with the juvenile type of xanthomatosis show osseous lesions and lipemia associated with pituitary disease. With the recent consideration given to the pituitary gland in insulin control it is possible that in the future one may find that the pituitary gland is the center of trouble in cases of xanthoma with lipemia.



## NECROBIOSIS LIPOIDICA DIABETICORUM Presented by DR JOHN F MADSEN, St Paul

V K, a woman aged 25, states that she has had diabetes for six years. The two cutaneous lesions appeared on the dorsum of the left foot and lower portion of the left leg early in 1934.

There are two plaques on the left leg which are violet at the periphery and yellow in the center. There is perceptible induration at the borders resembling granuloma annulare.

The cholesterol content of the blood was 208 mg per hundred cubic centimeters, and the sugar content was 281 mg (during fasting).

This case will be reported in detail later.

## NECROBIOSIS LIPOIDICA DIABETICORUM Presented by DR H E MICHELSON, Minneapolis

J M, a woman aged 23, states that she has had superficial ulcers on both legs for about seven years. At the time of the appearance of these lesions she was not aware that she had diabetes. About two years later she consulted a physician, who made a diagnosis of diabetes mellitus. During the past few years, the ulcers have healed with scarring on several occasions but have broken down again later.

There are several lilac-colored plaques on the legs below the knees. The larger lesions are scarred, and in some instances there are superficially eroded areas toward the periphery.

This case will be reported in detail later.

## NECROBIOSIS LIPOIDICA DIABETICORUM Presented by DR H E MICHELSON, Minneapolis

This woman, aged 38, was presented before the society a year ago. At that time she stated that she had had diabetes for three years and had noticed cutaneous lesions on the legs for almost a year. There were several waxy plaques situated bilaterally on the feet and ankles. These were violet, and some showed a yellow tint toward the center. Minute telangiectatic vessels were observed at the periphery of most of the lesions.

The patient was hospitalized for several weeks early in 1934 and received a careful dietary regimen supplemented by administration of insulin. Since the underlying diabetes has been under control, the cutaneous lesions have improved approximately 75 per cent.

## DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn. I have seen only one doubtful case of this rare disorder at the Mayo Clinic. I think the observations of Dr. Michelson and Dr. Laymon regarding the relation to other xanthomas are of definite practical importance.

DR CARL W LAYMON, Minneapolis (by invitation). At the University Hospitals my colleagues and I have had the opportunity of studying five cases of necrobiosis lipoidica diabetorum, in three of which ulcerated lesions were present. Within the past few months Urbach has noted a case with lipid infiltration in the ocular fundi. As to classification, we believe that the disease is only a local manifestation of a generalized lipodosis depending on an underlying diabetes. As time goes on, physicians will undoubtedly see cases of necrobiosis early enough to enable them to make the first diagnosis of the systemic condition, as was done in the case recently reported by Klaber, whose patient did not know she had diabetes until studies were made on account of the cutaneous lesions. One should also guard against making too narrow statements as to the histologic picture, since in our first case my co-workers and I observed many giant cells and intracellular deposits of lipid, two things which are not usually found.

DR H E MICHELSON, Minneapolis. I believe that before this condition is thoroughly evaluated there will be found a whole series of lesions, both clinical

and histologic, which will come under this general name. One will find on one end of this series a condition closely approximating xanthoma and on the other end a condition almost resembling gangrene. Since the publication of our article entitled "Necrobiosis Lipoidica Diabeticorum (Urbach), Dermatitis Atrophicans Lipoides Diabetica (Oppenheim) (*J A M A* **103** 163 [July] 1934), Dr Laymon and I have had additional experience with the condition, and we find that the microscopic picture is quite variable. At first we reported that no giant cells occurred, but since then have found giant cells. Professor Kren of Vienna, Austria, has sent me slides of microscopic sections, and these also show giant cells.

LOCALIZED MYXEDEMA Presented by DR H E MICHELSON, Minneapolis

Mr I F, aged 45, had experienced no trouble with his extremities until July 1931, six months after he underwent a thyroidectomy, when localized edema of the lower extremities appeared. A second thyroidectomy was performed in February 1932, but the individual lesions became larger and continued to progress until the last few months. During the patient's stay in the hospital the inactivity resulted in limited improvement of the eruption. No clinical or laboratory evidence of generalized hyperthyroidism or hypothyroidism could be discerned.

On both legs, particularly on the anterior portions, are elevated lesions varying in size from 1 to 5 cm. These lesions are moderately firm and rather rubbery. The surface is smooth, and the epidermis is somewhat thickened. There is no pitting edema of the extremities.

When the biopsy was performed, a mucoid material could be expressed from the wound. A section is presented, and stains for mucin gave positive results.

## DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn The term "localized myxedema" has justly been criticized as a poor one, but it is an expressive one from the pathologic standpoint The skin simply shows an extreme degree of myxedema with marked deposits of mucin throughout the cutaneous and subcutaneous tissue From the clinical standpoint these lesions of myxedema occur usually on the extremities and on localized areas after thyroidectomy, although the metabolic rate remains high

HONGKIN'S DISEASE OF THE SKIN Presented by DR S E SWEITZER, Minneapolis

This woman, aged 62, has complained of pruritus for the past four years, it is associated with enlargement of glands and loss of strength. The patient was treated unsuccessfully with antipruritic lotions and ointments, and the diagnosis was suspected only after biopsy of one of the enlarged axillary nodes. A biopsy of the skin confirmed the diagnosis, the histologic picture was typical. The individual cutaneous lesions first appeared about the neck and shoulders and consisted of many small, discrete elevated papules which were markedly pruritic. At present the lesions have spread to involve the greater portion of the skin.

## DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn. I agree that the histopathologic picture in the skin is that of true Hodgkin's disease with the presence of typical Dorothy Reed and Sternberg cells, which are characterized by prominent nuclei and large, prominent, densely staining nucleoli. These cells are not to be confused with benign endothelial and reticulum cells. True Dorothy Reed cells fulfil all the morphologic requirements of a malignant cell. I am in accord with the increasing number of dermatologists and pathologists who believe that Hodgkin's disease belongs in the group of lymphoblastoma. However, just as in the case of Kaposi's sarcoma or in the early stages of mycosis fungoides the histopathologic and clinical picture may be that of an inflammatory process, terminating, after a variable period of years, in sarcoma of different types or in other forms of lymphoblastoma.

I wish to call attention to the thickening of the palms of this patient. It is not an uncommon occurrence with any of the lymphoblastomas to see marked thickening or exfoliation of both palms and soles, this is often misinterpreted as keratoderma or eczema of different types

LUPUS ERYTHEMATOSUS (CHRONIC, DISSEMINATED) Presented by DR H E MICHELSON, Minneapolis

This man, aged 39, has an extensive cutaneous eruption of six years' duration which began on the scalp and face and gradually spread to involve the arms, palms, dorsa of the hands, soles and lower portions of the legs. He has been treated with local applications of various preparations, but only temporary results have been obtained.

There is an extensive eruption which in general consists of cyanotic red plaques, the surfaces of which are extremely hyperkeratotic. The palms and soles are especially involved by thick, warty efflorescences. On the dorsa of the hands, especially at the finger joints, there are purplish-red verrucous lesions, most noticeable in the periungual regions. When the firmly adherent scale is removed from the lesions, definite follicular plugging can be seen. Most of the hair has fallen from the scalp, though there is scarcely any scarring in that location. The face is involved by an atrophic, purple, slightly scaly plaque extending from the right cheek across the bridge of the nose. The mucosa is not affected, and the knees and elbows are free.

#### DISCUSSION

PROF FRANZ BLUMENTHAL, Ann Arbor, Mich (by invitation) The picture is unusual for lupus erythematosus. The lesions on the hands are unusual, but the clinical picture looks much more like that of lupus erythematosus than like that of pityriasis rubra pilaris.

DR HAMILTON MONTGOMERY, Rochester, Minn. This patient states that he was at the Mayo Clinic four years ago and that a diagnosis of lupus erythematosus was made. The sections presented were taken from an area on an arm, I believe, and showed a histologic picture strongly suggestive of pityriasis rubra pilaris because of the regular arrangement of parakeratotic cells in the corneal layer above the tips of the papillary bodies. Parakeratosis is usually not seen even in verrucous types of lupus erythematosus. The lesions on the palms and soles, and more especially the follicular lesions on the dorsa of the phalanges, also support the diagnosis of pityriasis rubra pilaris. I agree that the lesions on the face present all the features of lupus erythematosus. Dr Goeckerman reported one case in which both lupus erythematosus and psoriasis were present, as proved by the subsequent course, the lupus erythematosus clearing up and leaving the psoriasis (*M Clin North America* 15 1491 [May] 1932). It is possible that a similar coincidence of lupus erythematosus and pityriasis rubra pilaris is present in this case. I suggest a course of treatment with gold sodium thio-sulfate, this should have no influence on the lesions that resemble pityriasis rubra pilaris, if they are due to that disease.

DR JOHN F MADDEN, St Paul. I think that the accumulation of scales and debris on the feet is the result of poor personal hygiene. The patient states that he has not bathed his feet for the past eighteen months.

DR HENRY E MICHELSON, Minneapolis. I think that this is an unusual example of discoid lupus erythematosus in extenso. I believe that the microscopic picture has been altered by the fact that the patient has refrained from washing his hands and feet because he thought it made the condition worse. This has allowed an unusual accumulation of scales.

A CASE FOR DIAGNOSIS Presented by SAMUEL E SWITZER, Minneapolis

H B states that his eruption began five years ago on the left cheek and gradually spread until the entire face, neck and occipital portion of the scalp were

affected It has remained stationary for the past four years and is asymptomatic The patient has had two operations for tumor of the parotid gland

The skin of the face and neck and the posterior portion of the scalp are diffusely erythematous, and where local treatment has been applied there is scaling There is a partial loss of hair over the occiput There is also a poorly defined scaly, faintly red plaque over the left shoulder The skin over the hands appears slightly erythematous and somewhat thinner than normal

A section is presented

The Wassermann and Kahn tests were negative

#### DISCUSSION

PROF FRANZ BLUMENTHAL, Ann Arbor, Mich (by invitation) Atrophy and hyperkeratosis are present I believe that this is a case of lupus erythematosus

#### ADENOMA SEBACEUM (PRINGLE) AND SUBUNGUAL AND PERIUNGUAL FIBROMAS Presented by H E MICHELSON, Minneapolis

T L, a youth aged 19, states that when he was 4 years old papular lesions began to appear around the nose and that the eruption progressed until it reached its present extent several years ago He states that the lesions bleed easily when injured The lesions around the toe-nails have been present as long as the patient can remember The father of this boy had a similar eruption on his face in his youth It was treated by cauterization He also has small papillomas around the toe-nails

There are a large number of soft papules on the chin, cheeks and nasolabial areas, and a few scattered lesions are present on the neck and forehead The color varies from brown to bright red On the chin the lesions are so closely grouped that the surface resembles a large raspberry On nearly every toe are one or more firm papillomas of various sizes, the largest being 3 mm in diameter They have the color of normal skin, and they show no tendency to bleed when injured These fibrous lesions are firmly attached to the tissues immediately adjacent to any portion of the nails

General examination failed to show any evidence of Recklinghausen's disease or tuberous sclerosis The mentality is normal

A section is presented

#### DISCUSSION

DR F W LYNCH, St Paul The relationship between subungual fibromas and adenoma sebaceum was discussed by Enokow (*Dermat Wchnsch* 97 1061 [July] 1933) He regarded both conditions as a manifestation of Recklinghausen's disease Dr Brock discussed the relationship of tuberous sclerosis to adenoma sebaceum before this society some time ago There is no evidence of any neurologic involvement in Dr Michelson's patient

#### SCLERODACTYLIA Presented by DR H E MICHELSON, Minneapolis

A C, a woman aged 60, first noticed stiffness in her fingers and toes five years ago Gradually loss of motion of these structures has occurred, simultaneously with shrinking and hardening of the overlying skin A sympathectomy on the right side was performed in November 1934, but little or no change in the condition resulted

The skin covering the fingers and toes is firm and shrunken Motion is greatly limited, the digits being scarcely movable There are no ulcerations The nose is abnormally pointed, smooth and firm to palpation Tiny telangiectatic vessels are seen coursing from the cheeks over the bridge and tip of the nose

#### DISCUSSION

DR ASHTON L WEISH, Rochester, Minn Besides sclerodactylia this patient has a sclerodermatous process on the face and neck She did not remove her

clothing, hence the remainder of her body could not be examined. The unusual features in this case are the peculiar discrete, telangiectatic macules over the nose, cheeks and chin, these are from the size of a pinhead to that of a pea. Some of the lesions fade out when pressure with the diascopé is applied, others do not. My co-workers and I recently had a patient with scleroderma and sclerodactylia at the Mayo Clinic who presented telangiectatic lesions of this type on the face, palms and forearms. This type of telangiectasia is distinctly different from the usual diffuse type of telangiectasia so often associated with scleroderma. Our patient stated that she had exacerbations and remissions of these lesions but that she was never entirely free from them. At the sites of some of these telangiectatic macules the atrophy was somewhat more marked than in the surrounding sclerodermatous area.

I made a brief survey of the literature on this subject and I found the condition described in the *Handbuch der Haut- und Geschlechtskrankheiten*, where Lwien-Heller is credited with the original description. References are made to other descriptions by several German and French and by a few English authors. F. Parkes Weber and Bernard Meyers (*Proc Roy Soc Med [Cln Sect]* 14 52, 1921) described a similar type of telangiectasia associated with lesions of the lips and oral mucous membrane in a patient with scleroderma and sclerodactylia. Rothwell (*ARCH DERMAT & SYPH* 10 96 [July] 1924) presented a patient with this condition before the Section of Dermatology and Syphilis of the New York Academy of Medicine, on Feb 5, 1924.

**SARCOID (DARIER-ROUSSY)** Presented by DR. SAMUEL E. SWEITZER, Minneapolis

A. W., a woman aged 42, noticed a lesion on the right leg about three years ago. It appeared near the knee beneath the skin, grew slowly and then became visible on the surface as a scaly patch surrounded by smaller satellite lesions. A second lesion appeared about two and one-half years ago, near the ankle. The lesions are tender on pressure. The patient was seen first in December 1934, she was hospitalized at that time. She received fever therapy by means of diathermy. The lesion near the ankle disappeared almost immediately. The patient had tuberculosis of the left hip at the age of 2½ years. An uncle and aunt and two cousins died of tuberculosis.

At present there is a cyanotic plaque measuring 2 by 3 cm. on the lateral surface of the left knee. This lesion is surrounded by tiny satellite nodules. All parts of the lesions are firm to palpation.

A section is presented.

The Wassermann and Kahn tests and the Mantoux test gave negative results. Roentgenograms of the chest showed no abnormalities.

#### DISCUSSION

PROF. FRANZ BLUMENTHAL, Ann Arbor, Mich. (by invitation). Lupus vulgaris is a common disease in Germany. Apparently it is rare in the United States. The other forms of tuberculosis of the skin in the United States seem to occur as frequently as in Europe.

It is certain that in the majority of cases lupus is a localization secondary spread from an internal focus. In spite of that, I think it is wise to treat the condition locally, because if one removes the external focus, much of the infectious agent is destroyed and the patient becomes able to protect himself much more efficaciously against the infection.

Concerning the mechanism of the therapeutic action of heat in cases of tuberculosis of the skin it would be difficult to explain exactly every detail. It is known that complicated reactions occur in the skin after application of light and heat. Certainly the rays of light have a marked bactericidal action and a curative effect in cases of tuberculosis of the skin. The therapeutic effect is due to an inflammatory reaction of the tissue, and it is possible that heat acts in the same way.

In my opinion it is not possible to compare the condition caused by the gonococcus with that caused by the tubercle bacillus, because the gonococcus is highly sensitive to heat whereas the tubercle bacillus is highly resistant

DR HAMILTON MONTGOMERY, Rochester, Minn The histologic section in Dr Sweitzer's case shows epithelioid tubercles not only just beneath the epidermis but also extending deep into the subcutaneous tissue, thus presenting features of both the Boeck and the Darier-Roussy type of sarcoid Not long ago Dr Goeckerman emphasized the fact that the various types of sarcoid, including lupus pernio, merge and stated that sharp distinction between various types often proves to be artificial

DR R R SULLIVAN, Rochester, Minn In connection with the treatment of tuberculosis, I wish to refer to the work of Lomholt at the Finsen Institute (*Arch f Dermat u Syph* **170** 467 [Sept] 1934) Dr Lomholt reported having obtained favorable results with esters of chaulmoogra and hydnocarpus oil in the treatment of fourteen patients with Boeck's sarcoid, three with granuloma annulare and four with mycosis fungoides In the treatment of sarcoid, complete or almost complete disappearance of the nodular infiltrate was brought about in most of the patients, and symptomatic improvement was noted in the remainder Whether or not esters of chaulmoogra and hydnocarpus oil are an effective therapeutic agent in tuberculosis of the type mentioned will be determined only by their wider use in a larger, well controlled series of cases I agree with Professor Blumenthal about the results reported by Dr Rusten, i e., that the treatment must be used in a larger series of cases over a longer period before an attempt is made to evaluate the therapy

DR H E MICHELSON, Minneapolis I am in favor of treating tuberculosis of the skin locally, and any method that has been proved to be valuable and sensible is indicated My reason for this is that if one can remove a certain focus of tuberculosis it may be sufficient to enable the patient to hold in check or even overthrow any remaining internal foci In cases of lupus it has been definitely shown that an effective external therapy greatly improves the general health of the patient and facilitates the management of constitutional disorders

DR ELMER RUSTEN, Minneapolis This patient was given four general treatments by diathermy with temperatures between 104 and 105 F After two treatments the lesion had begun to involute, and at the end of four treatments it had disappeared This treatment was instituted because of the work done by Dr George R Duncan and his co-workers at the Glen Lake Sanatorium, Oak Terrace, Minn, in which he had demonstrated that in vitro human tubercle bacilli grow at temperatures between 96 and 100 F, grow poorly at temperatures from 100 to 104 F and do not grow at all above this temperature Various types of cutaneous tuberculosis are being treated at the present time, and results will be reported later

#### CASES PRESENTED BUT NOT DISCUSSED

LUPUS VULGARIS Presented by DR JOHN F MADDEN, St Paul

SECONDARY SYPHILIS (PUSTULAR) Presented by DR SAMUEL E SWITZER, Minneapolis

PARAPSORIASIS Presented by DR JOHN BUTLER, Minneapolis

ACRODERMATITIS CHRONICA ATROPHICANS Presented by DR H E MICHELSON, Minneapolis

DARIER'S DISEASE (TWO CASES) Presented by DR H E MICHELSON, Minneapolis

PIODERMA (ULCER OF THE LEG) Presented by DR H E MICHELSON, Minneapolis

LYMPHOHEMANGIOMA Presented by DR H E MICHELSON, Minneapolis

ADENOMA SEBACEUM AND RECKLINGHAUSEN'S DISEASE Presented by H E MICHELSON, Minneapolis

BLASTOMYCOSIS (SYSTEMIC) Presented by DR H E MICHELSON, Minneapolis

SYRINGOCYSTOMA Presented by DR H E MICHELSON, Minneapolis

A CASE FOR DIAGNOSIS (MYCOTIC DERMATITIS? DERMATITIS HERPETIFORMIS?)  
Presented by DR H E MICHELSON, Minneapolis

URTICARIA PIGMENTOSUM Presented by DR H E MICHELSON, Minneapolis

TUBERCULOSIS COLLIQUATIVA Presented by DR H E MICHELSON, Minneapolis

MYCOSIS FUNGOIDES Presented by DR H E MICHELSON, Minneapolis

BALANITIS XEROTICA OBLITERANS Presented by DR H E MICHELSON, Minneapolis

PURPURIC LICHENOID DERMATITIS Presented by DR H E MICHELSON, Minneapolis

CARCINOMA OF THE BREAST WITH CUTANEOUS METASTASES Presented by DR  
JOHN F MADDEN, St Paul

MALIGNANT MELANOMA Presented by DR H E MICHELSON, Minneapolis

PEMPHIGUS FOLIACEUS Presented by DR H E MICHELSON, Minneapolis

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## NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

FRANK C COMBES, M D, *Secretary*

*Oct 1, 1935*

MAX SCHEER, M D, *Chairman*

A CASE FOR DIAGNOSIS (PEMPHIGUS VULGARIS?) Presented by DR BOTHO  
FELDEN

N O, a woman aged 65, is presented from the New York Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, where she was first seen on Sept 6, 1935. She had been in good health until then. The present condition started about four weeks ago with itching and burning on the face and neck without any apparent reason. The patient states that she has not taken any medicine. After she applied a 2 per cent concentration of ammoniated mercury in boric acid ointment, prescribed by her physician, the present eruption appeared. The eruption consists of numerous discrete, round and oval bullous lesions. Some of them show a slight tendency to grouping. There are also numerous denuded areas, some of which are covered with adherent crusts. On the inside of the lower lip there are two eroded patches. The lesions are from the size of a split pea to that of a cherry.

The Wassermann reaction of the blood was negative. Complete examination of the blood showed 74 per cent hemoglobin (9.5 Gm per hundred cubic centimeters), with 4,200,000 red cells and 7,400 white cells. The differential count showed 3 per cent immature polymorphonuclears, 49 per cent old polymorphonuclears, 30 per cent lymphocytes, 8 per cent monocytes, 1 per cent basophils and 8 per cent eosinophils. The red blood cells were normal. A differential count (50 cells counted) of the contents of a bleb showed 35 per cent polymorphonuclears, 3 per cent lymphocytes, 1 per cent monocytes and 61 per cent eosinophils. A cutaneous test with a 50 per cent solution of potassium iodide produced erythema, vesicles and pustules, amounting to a 2 plus reaction.

## DISCUSSION

DR SIGMUND POILITZER. I have no doubt that the disorder is pemphigus vulgaris. Any hesitation in making this diagnosis can arise only from the facts that the disease is in an early stage and that there are few lesions. However, the lesions are typical.

DR EUGENE TRAUOGT BERNSTEIN. The eruption involves areas accessible to the patient's hands. There are bullae on the normal skin, but the striking part of the picture is that there are also some grouped lesions and scaliness. It is difficult to determine the differential diagnosis in this case. One should first consider the possibility of dermatitis herpetiformis in spite of the unusual location for this disorder. Moreover, the lesions may be neurotic excoriations in association with pemphigus hystericus. The location is typical of that of a psychodermatitis, the patient is nervous, and frequently patients with neurotic excoriations exhibit bullae and vesicles, even on the mucous membranes.

## FOX-FORDYCE'S DISEASE. Presented by DR ANTHONY C. CIPOLLARO

E. G., a Negress aged 23, single, born in Brazil, a domestic, is presented from the New York Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. Itching about the anus developed in the spring of 1933. After approximately six months the pruritus extended to involve the vulva. In April 1934 suspension of the uterus and appendectomy were performed at a local hospital for discomfort in the lower right quadrant of the abdomen and a vaginal discharge. Relief was not obtained, and the patient returned to this hospital in October 1934, she states that at that time a diagnosis of "inflammation" of the stomach, salpingitis and oophoritis was made. In November 1934 severe itching developed about the umbilicus, over the sternum about the nipples and in the axillae. Shortly after this the patient discovered an eruption distributed in these locations. When she examined the pubic region she found a similar condition there. The patient has noticed that symptoms show a tendency to develop in hairy regions. The eruption is accompanied by paroxysms of intolerable itching. Nervousness, excitement and tension precipitate or exaggerate the symptoms. Heat also increases the itching and has forced the patient to give up her work as a cook. She also suffers from hay fever.

The patient presents an eruption of uniform, discrete, firm, smooth, round, shiny, skin-colored to slightly pink papules, varying in size from that of an ordinary pinhead to that of a glass pinhead. The lesions are distributed in the axillae, around the nipples, over the neck, in the presternal region and over the lower portion of the abdomen, pubis and labia. Some of the lesions seem to have a minute central punctum, others have a dark-colored plug. A number are pierced by hairs. The growth of hair is sparse in the involved regions. The lesions in the axillae are superimposed on slightly thickened infiltrated skin and in places have a linear distribution.

Examinations in the medical and gynecological clinics gave negative results. The blood pressure was 110 systolic and 70 diastolic. The Wassermann and Kahn tests and the urinalysis gave negative results. A biopsy confirmed the diagnosis.



## DISCUSSION

DR ANTHONY C CIPOLLARO There are several unusual features about this case which I wish to point out. The distribution of the lesions is extensive. Lesions occur on the sternum and neck—locations which are not generally affected by this condition. The cases reported occurred mostly in white persons. This patient is a Negress. It is significant that most of the cases of Fox-Fordyce's disease occur in women. There seems to be some disagreement in regard to the particular glands affected by this disease. The consensus is that the pathologic changes involve the apocrine rather than the eccrine glands. Its relationship to neurodermatitis and to other allergic diseases needs to be studied. Many of the histologic specimens of Fox-Fordyce's disease resemble specimens of neurodermatitis. This patient has hay fever. Because of the intense pruritus and the suffering it causes, I should appreciate suggestions for treatment. Roentgen radiation controls the pruritus temporarily.

DR SIGMUND POLLITZER I agree with the diagnosis of Fox-Fordyce's disease. The location of the papular pruritic lesions in the axillae, in the pubic region and in a line from the navel to the pubes is characteristic. As a rule, there is much more evidence of scratching and of secondary changes than in this case. The consensus is that the disorder is due to a disturbance in the apocrine glands and, underlying this, an endocrine dysfunction. The apocrine glands have long been known as odoriferous glands and are related to the sexual function. As to treatment, I advise a thorough study of the endocrine function and local application of antipruritic agents, especially small doses of roentgen radiation.

DR CHARLES WOLF I wish to make a suggestion in regard to therapy. I have had an opportunity of treating two or three patients with Fox-Fordyce's disease in private practice. Persistence in using roentgen radiation is a prerequisite for success. It is easy for the patients to get discouraged because they do not see rapid improvement. Filtered radiation should be used. I employ 500 roentgens filtered with 3 mm of aluminum which is equivalent to what was formerly called an erythema dose. Three such doses at intervals of one month are required. There is no contraindication to giving more than three doses if improvement is taking place and there are no untoward changes in the skin.

DR HERMANN GOODMAN There have been, I think, sixty-five cases of this disease reported since Dr Fox and Dr Fordyce first reported their case. Like every one else, I have been impressed by the fact that only two male patients have been regarded as having Fox-Fordyce's disease. That may explain the suggestion just made by Dr Pollitzer of studying the endocrine function in order to find out something about this condition. Incidentally, in the reported cases in which sufficient roentgen therapy was given, itching persisted despite administration of sufficient radiation to cause a dermatitis. My report on the Fox-Fordyce syndrome was published in the *Acta dermato-venereologica* (7:509, 1927).

DR SIGMUND POLLITZER The excellent section under the microscope shows the large apocrine glands (modified sweat glands), and, corresponding to the clinical picture, the unusual freedom from secondary changes.

## DARIER'S DISEASE Presented by DR VAN ALSTYNE H CORNELI

G L, a girl aged 17, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. When she was first seen, on Aug 5, 1935, she had had an eruption on both sides and the back of the neck for five weeks. Examination showed lichenified areas consisting of closely aggregated pinhead-sized hard brownish papules and some vesicular areas. There were hard, scaly papules over the scalp. On the forehead were a few scaly areas. There was no itching. A biopsy made on Aug 19, 1935, showed Darier's disease. Since the first examination the eczematous lesions on the back of the neck have cleared up completely. The lesions on the sides of the neck persist. The patient received two superficial roentgen treatments, one on September 4 and one on September 13.

The Wassermann reaction of the blood was negative on August 20.

## DISCUSSION

DR SAMUEL M PECK I am much interested in this case. My conception of Darier's disease is that it belongs to the nevus group, is familial in its tendency, runs a chronic course and is very difficult to eradicate completely. However, recently I had occasion to study a patient with an acute eruption such as that exhibited by Dr Cornell's patient. I could not quite make up my mind as to the diagnosis, and I asked Dr Rosen to see the patient with me. He diagnosed the condition as an acute form of Darier's disease. Much to my surprise, the histologic section seemed to bear out that diagnosis. In spite of the similarity in histologic picture between the acute eruption exhibited by Dr Cornell's patient and that shown by my own patient with Darier's disease, I still think that the two conditions must be differentiated. It is evident that the acute process is not a nevus and responds fairly rapidly to roentgen therapy. The only point of similarity seems to be in the histologic picture. These acute eruptions are not, in my opinion, true Darier's disease.

DR MAX SCHEER The remarks made by Dr Peck are rather interesting. About twenty years ago I looked up all the literature I could find on Darier's disease. I was particularly interested in ascertaining the duration of the disease at the time the patients were first seen. At that time I could not find a single report of a case in which the disease had been present less than two years. In the majority of cases the duration was eight, ten or more years. I was interested because at that time I had a patient with a condition which histologically was Darier's disease but which had been present for only one month. The early stages do not resemble the late stages at all. Clinically, of course, the late stages reproduce the typical picture described in textbooks. The early stages do not. In the early stages the disease responds readily to roentgen therapy, whereas in the late stages it does not. In the case to which I referred the condition cleared up under roentgen therapy. The dyskeratosis which is present in the early stages is helpful because in the other diseases in which dyskeratosis exists, for example, in molluscum contagiosum, the clinical picture is different. There are a number of other conditions in which this dyskeratosis is present, but clinically they are different from Darier's disease. One cannot confuse them. Perhaps Dr Cornell can give more details on the histologic picture.

DR VAN ALSTYNE H CORNELL I cannot give details about the histologic picture. Dr Satenstein saw the sections.

DR SIGMUND POLLITZER I was studying in Paris shortly after Darier described the disease since called by his name, and I still have a section made in Darier's first case. The peculiar round cells with double contours were regarded as protozoan bodies. In fact, the diagnosis of psorospermiosis was made by Balbiani and Melassez. At the clinical meeting in connection with the International Congress of Dermatology and Syphilology in Copenhagen in 1930 six or eight patients with this disease were presented, and in the discussion Darier deprecated the association of his name with a disease which, he said, had proved to be neither psorospermiosis nor a follicular or vegetative process. The "psorosperms" are, of course, examples of dyskeratotic cells. The disease belongs in the group of nevi, though the lesions, as is often the case with diseases which exhibit a congenital tendency, may not manifest themselves till after one or two decades of life. There is no cure for the disorder.

DR MARION B SUZBLER I wonder whether any of the members noticed the lesions which this young woman has on the dorsa of the hands, on the ulnar surface. They look much like verrucae planae. Lesions of this type are not infrequently seen in cases of Darier's disease.

PIGMENTED EPITHELIOMA Presented by DR RICHARD J KELLY

P C A woman aged 63 born in Italy, is presented from the Vanderbilt Clinic. She has had a pigmented 'mole' on the left temporal region for the past fifteen years. As a result of injury the lesion began to grow rapidly during the past

three to four months. It now measures 2.5 by 3.25 cm, has raised, bluish-black edges and is ulcerated in the center. A portion of the border shows a rolled edge with a pearly luster. The possibility of melanoma was considered. There is a suggestion of a palpable gland in front of the lobe of the left ear in the parotid region. There is also a movable gland, about 2 by 3 cm in diameter, in the submaxillary region but the patient's daughter states that this has been present for as long as she can remember, and the patient says it has been present since before her marriage.

Biopsy showed a pigmented basosquamous cell epithelioma. Roentgenograms of the chest and skull showed no pathologic changes. The urinalysis and Wassermann test of the blood gave negative results. The urine did not contain melanin.

#### DISCUSSION

DR C. F. MACHACEK: The lesion is a typical basal cell epithelioma with perhaps some squamous characteristics.

DR SAMUEL M. PECK: It is interesting in these cases to try to determine histologically whether one is dealing with the pigmented benign tumors of the skin which Bloch described or with a lesion which can be classified as a pigmented basal cell epithelioma. When Bloch described the two types of tumor which are sometimes known as Bloch's pigmented epitheliomas, he described one type in which there is a predominance of basal cell elements and one in which there is a predominance of the dendritic elements. It has been a rule in histologic classification of pigmented tumors that when cells undergoing mitosis are found the tumor is regarded as malignant. A few years ago I found that the cell in the process of mitosis does not give a positive dopa reaction. Some dendritic cells are active pigment-forming cells, that is why mitotic figures are not found in those elements. Dr. Eller and others in writing on this subject have not been clear as to whether they were describing the tumors Bloch described or the pigmented basal cell epitheliomas. In a recent article Montgomery (*Radiology* 25:8 [July] 1935) gave a good summary of the subject. It is his opinion that what Bloch described was not a basal cell epithelioma but an intra-epidermal epithelioma with pigment.

DR RICHARD J. KELLY: The question was simply whether this lesion is melanocarcinoma or a basal cell carcinoma. From the history and the signs presented I cannot regard it as a basal cell epithelioma with pigmentation or treat it as such.

A CASE FOR DIAGNOSIS (DERMATITIS?) Presented by DR JOSEPH L. MORSE

W. G., a man aged 42, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has had a dermatitis around each axilla for the past six months. The condition improves but flares up suddenly, without any apparent reason. The patient says that the exacerbations are usually preceded by itching, but he says that he does not scratch or rub the involved parts to any great extent. There is no history of application of any external irritants or of ingestion of drugs. Examinations for fungi have given negative results.

Improvement resulted from roentgen irradiation and application of a bland ointment, but the disorder reappeared. Mild ointments of chrysarobin and anthralin (di-hydroxyanthranol) improved the condition at first, but after several days they irritated it and their use had to be discontinued. Almost anything seems to help for a time, but relapses continue to occur.

The patient presents a fairly sharply outlined area of dermatitis on the chest and on the side of each arm around the axilla. The axillae are perfectly free from any eruption, but there is a moderate degree of hyperhidrosis. At the time of the flare-ups the involved areas become vesicular and exudative.

The diagnosis is dermatitis of unknown etiology.

## DISCUSSION

DR JOSLPH L MORSE The disorder looks like a simple dermatitis. It gets better and worse without reason. I am confident that the patient is not a malingerer. He was well yesterday when I saw him and told him to come here. Tonight the eruption has flared up again.

The question of the use of irritant chemicals in the laundry has been considered, but I do not see how this factor can arise because the patient has worn gauze under his shirt since I have been seeing him. As I said before, I thought this case was simple, but it seems to me that the simple problems in dermatology are the hardest to solve. The patient is presented not so much for diagnosis, because I cannot see any other diagnosis than dermatitis (the condition looks like dermatitis venenata to me), as because I should like to hear what the members suggest in regard to treatment. The hyperhidrosis of the axillae has disappeared as a result of roentgen treatment.

DR HENRY D NILES I agree with what Dr Morse said as to the diagnosis. I do not think that there is any question of dermatitis venenata. I also agree with him that the apparently simple eruptions are often the hardest to cure. Since I saw his patient I have tried to think of any possible irritant that might cause this eruption. I have been unable to think of any. I consider it striking that the axilla itself is not involved. There is a patch above and below the axilla. I cannot make any suggestion, but I believe, as Dr Morse does, that the eruption is due to some external irritant.

DR SIGMUND POLLITZER This seems to me a perfectly obvious case of allergic dermatitis with a typical history. The rather severe circumscribed dermatitis yields to slight treatment, remains quiescent for a while and then abruptly flares up again. The patient manifestly does something that produces the eruption. Careful inquiry may afford a clue as to the cause and the usual cutaneous tests may reveal the peccant element. These cases always demand careful detective work. Meanwhile I should advise treatment with moderate doses of roentgen radiation, which may bring about a change in the specific sensitivity.

DR MARION B SULZBERGER I cannot throw any light on this case, but I can add two more cases just like this one to the records. One patient was seen in Europe and the other, a woman referred by Dr Charles Rein, was seen about a year ago in the office of Dr Wise. In these cases my co-workers and I also suspected that the eruption was an artefact or malingering. In fact, in Dr Rein's case there was a strong suspicion that malingering was responsible, because a question of compensation was involved. The patient, I believe, claimed to have originally had a burn. In these cases the disorder was clinically identical with that presented by Dr Morse's patient.

The question of the sparing of the axilla is, of course, interesting, but the phenomenon is not unusual. If one knew why the axilla is spared in so many of the dermatoses involving the region around the axilla one would be a little further in the study of factors producing immunity in these conditions. One can now only suppose that it is a question of the secretion of the glands in that region.

As to treatment, I suggest that which was used on the patient I saw recently, namely, application of an occlusive dressing, for instance with a bandage of zinc oxide gelatin over the entire shoulder and axilla. If possible, I should hospitalize the patient.

It might have proved interesting to obtain some of this patient's sweat and use it in patch tests.

DR LOUIS TULLIAN I have observed several similar cases especially in women with pendulous breasts the apposing surfaces of which rub against each other, causing a good deal of perspiration. I have seen the same thing on the inner side of the thighs. This patient has an eruption on the apposing surfaces of the arm and chest such as one sees in intertrigo. He has the same involvement on both sides. He could not produce artificially an eruption as well defined as

that which is present on these four sites. Besides this, these patients frequently have a staphylococcic infection, giving the appearance of an infectious eczematoid dermatitis. The best results in these cases are obtained by applications of gentian violet or brilliant green covered with dressings of collodion. The disorder usually clears up in about a week. I am certain that if this procedure is followed the condition will clear up in a week. That has been my experience.

DR E. MILES STANDISH, Hartford, Conn. I had a patient this summer whose condition was almost the exact counterpart of that exhibited by Dr. Morse's patient. I tried all sorts of patch tests, but the results were negative. In hot weather, when the patient perspired considerably and his shirt became moist, the eruption was worse. The only way in which he obtained relief was by removing his shirt and allowing the area to dry as much as possible.

DR ADOLPH ROSTENBERG. I wish to mention a case in which clinically the eruption looks exactly like that exhibited by this patient and which has puzzled me for more than four years. This patient has lesions around the neck, sometimes the eruption consists of a few patches, and sometimes there is a circular band around the entire neck. The condition shows exacerbations and remissions. Sometimes an outbreak clears up after one roentgen treatment, the condition remaining quiescent for about two weeks and then recurring. I also tried to find the cause, I examined the patient's collars, subjected him to patch tests and carried out all the investigations I could think of, but I have not been able to ascertain the cause of the disorder.

DR JOSEPH L. MORSE. I have tried everything mentioned in the discussion except the occlusive dressing. I have obtained almost a complete cure with gentian violet. Then the eruption recurred, being as severe as ever, though the gentian violet was still applied. The patient has gone without a shirt nearly all summer, without benefit. He will do anything to get well. I considered the possibility of allergy to food and ordered a restricted diet. The patient has even fasted, but the eruption broke out just the same. I do not know exactly what Dr. Sulzberger meant by the patch tests with sweat. It seems to me that if sweat were a cause, the fact that the patient had not been sweating for about a month should cause the eruption to clear up. He does not sweat excessively any more. I believe that the patient gets some sensation in the involved areas, and either in his sleep or while he is awake precipitates an attack by rubbing. The condition is not intertrigo. It goes all the way around the shoulder. I shall try an occlusive dressing.

#### DESQUAMATION OF THE HANDS Presented by DR EUGENE F. KELLEY

A B, a woman aged 33, born in the United States, is presented from the Vanderbilt Clinic. She was first seen on Sept. 30, 1935, at which time she stated that wrinkling of the hands had been present eleven days before. This wrinkling became more pronounced, and on the seventh day she was able to remove the horny layer en masse in a way similar to removing gloves. The hands are perfectly normal. The plantar surfaces of the toes are slightly hyperkeratotic. The ankles are swollen. The patient states that she has not taken any drugs and has not handled irritating substances. She has not been ill in the past three and a half years.

A specimen is presented.

#### DISCUSSION

DR MAX SCHLEER. This is a remarkable specimen.

DR EUGENE F. KELLEY. I presented this specimen to see whether any of the members can suggest a possible cause for this rapid and complete casting off of the horny layer of the hands. I saw the patient for the first time yesterday. She may have had scarlatina.

DR MIHRAN B. PAROUNAGIAN. I should make a diagnosis of erythema scarlatinoides. I have seen two cases, but this is about the best example of this condition that I have seen.

DR SIGMUND POLLITZER This is indeed a rare and perfect specimen. The literature refers to a small number of cases of shedding of the skin, and in some of them the desquamation occurred periodically. One is reminded of the shedding of the epidermis in some of the lower vertebrates.

DR MAX SCHEER I wish to ask Dr Kelley whether the nails were also shed.

DR EUGENE F KELLEY The finger-nails and toe-nails are perfectly normal. It is my impression that the feet will exfoliate.

DR OSCAR L LEVIN The specimen presented is unique. In my own experience I have never previously observed so marked an example of this condition. Recently I treated a patient who was hospitalized. This patient presented a severe toxic erythema and shed large sheets of epidermis, but the desquamation was in no wise comparable to that revealed in this specimen.

#### REPORT ON A CASE PREVIOUSLY PRESENTED DR OSCAR L LEVIN

At the meeting of April 2, 1935 (*ARCH DERMAT & SYPH* **33** 165 [Jan] 1936), I presented for diagnosis of her condition a woman with a large chancre-like lesion on the lower lip. There were smaller lesions on the eyelids and lip. When the patient was presented various suggestions were made as to the diagnosis and treatment. It was suggested that active antisyphilitic therapy should be administered immediately and that a piece of tissue be removed for microscopic study. Several other procedures were outlined. Since the patient was presented she has been under my observation, and repeated examinations for spirochetes have given negative results. Wassermann tests have been negative, and bacteriologic examinations have revealed no specific micro-organisms. The lesion was treated merely by application of boric acid ointment, and after several weeks it disappeared completely. There has been no recurrence. I believe that this disorder resembles the condition described by Erich Hoffmann (*Arch f Dermat u Syph* **170** 403 [Sept 14] 1934). It suggests the picture of syphilis, tuberculosis, sporotrichosis, mycotic infection, tularemia and neoplasm. Dr Chargin recently told me of a patient whom he was treating who had lesions like those exhibited by my patient.

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FRANK C COMBES, M D, *Secretary*

*Nov 6, 1935*

MAX SCHLER, M D, *Chairman*

#### KAPOSI'S HELMORRHAGIC SARCOMA Presented by DR HENRY D NILES

F K, a man aged 62, born in Czecho-Slovakia, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption on the lower part of the left leg of twenty months' duration. The eruption started with a flat, purplish-red spot, which gradually enlarged and became hard, elevated and warty. There has been no pain, but itching is severe at times.

On the inner aspect of the lower portion of the left leg is a rather sharply outlined, palm-sized, raised, infiltrated dull purplish-red patch. This is partly covered by thick warty crusts beneath which are many small red protuberances. There are no other lesions on either leg but there are several rather large varicose veins.

The Wassermann and Kahn tests of the blood and examination of the urine gave negative results. A biopsy performed on Aug 23 1935, showed many dilated and proliferating blood vessels, increased connective tissue consisting of many spindle-shaped cells, and several deposits of brown granular pigment.

Since Aug 29, 1935, the patient has received two treatments with  $\frac{1}{4}$  skin unit (75 roentgens) of unfiltered radiation and three treatments with  $\frac{1}{4}$  skin unit (22½ roentgens) filtered with 3 mm of aluminum. These have caused considerable improvement. The lesion has become softer, less warty and paler.

## DISCUSSION

DR SIGMUND POILITZER On the basis of the histologic examination, notwithstanding the fact that this is an unusual but not impossible clinical picture, I should say that the disorder is probably Kaposi's sarcoma.

DR HERMAN GOODMAN I should have called it hypertrophic lichen planus.

DR HENRY D NILES I think that this case is interesting because in the beginning there was an atypical picture of Kaposi's sarcoma. The disorder has improved unusually rapidly with small doses of roentgen radiation. The histologic picture is typical of Kaposi's sarcoma.

## PUSTULAR PSORIASIS Presented by DR ISADORE ROSEN

S L, a woman aged 52, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. An eruption appeared on the feet five and one-half months ago, and a few days later similar lesions appeared on the hands. There is no itching. The patient has never had a similar eruption previously.

On the sole and inner aspect of the right foot, on the inner aspect of the right great toe and on the terminal phalanges of all the toes of the right foot there are many grouped, subepithelial, pinhead-sized pustules. The patches are sharply outlined, erythematous, scaly and circinate. All the toe-nails are thickened and discolored. Paronychia is present. There are some scaling and maceration between the toes. On the left foot there are similar but less marked lesions. The palms show similar lesions. The finger-nails of the right hand show changes. There are no lesions on the scalp, elbows or knees. No focal infections have been found.

The Wassermann reaction of the blood was negative. Examinations of the hands and feet for tinea on Aug 25 and on Oct 28, 1935, gave negative results on slides and cultures. Intradermal tests made on August 30 gave the following results. A test with 0.1 cc of a 1:100 dilution of oidiomycin produced a wheal 1.5 cm in diameter and an area of erythema 5 cm in diameter in forty-eight hours, a test with 0.1 cc of a 1:30 dilution of trichophyton produced a negative reaction in forty-eight hours but a positive delayed reaction. Studies of the cholesterol content of the blood serum were made. The results compared with the normal amounts are given in the tabulation.

	Normal Content	Content in Blood Serum of Patient
Total cholesterol	194 to 230 mg per 100 cc	285 mg per 100 cc
Cholesterol esters	133 to 171 mg per 100 cc	115 mg per 100 cc
Free cholesterol	53 to 65 mg per 100 cc	170 mg per 100 cc
Free cholesterol	24 to 32 per cent	59 per cent

A specimen for biopsy was taken on Oct 30, 1935, from the sole of the right foot. The report by Dr Satenstein was as follows: "The epidermis is irregularly acanthotic. The rete pegs are broadened in part. The granular layer is increased in the middle of the section. There is a cavity covered by a thin horny layer. The basis comprises most of the prickle cell layer. The contents consist of fibrin, polymorphonuclears and remnants of prickle cells. The basal layer is disturbed and there is immigration of cutis cells. Under this part in the cutis there is a diffuse cellular infiltrate composed of small round and connective tissue cells. There is a similar focal cellular infiltrate around the vessels."

## DISCUSSION

DR DAVID BLOOM I agree with the diagnosis

DR GEORGE C ANDREWS I believe that it remains to be proved that this patient's condition is pustular psoriasis. She shows no signs of psoriasis, she has never had psoriasis, and there is no history of psoriasis in her family. She has a pustular eruption on the palms and soles, and I think that further work will have to be done to establish what the disorder is. I recommend that blood counts, examination of the teeth and other studies be made.

DR DAVID L SATENSTEIN There is rather a curious thing about this type of dermatosis. My co-workers and I have observed twenty or twenty-five cases. Microscopically the disorder has none of the characteristics of psoriasis. The location of the pustules or vesicopustules is always the same, irrespective of whether the tissue comes from the plantar or from the dorsal surface, from the hands or from the feet, I have seen similar changes in one specimen from the region of the elbow. In all the cases there is exactly the same pathologic picture, that is, a picture of a dry type of chronic eczema, and in the epidermis there is a fairly large, sharply margined cavity filled with polymorphonuclear leukocytes. I believe that this condition is a definite entity, about the etiology of which I have no concepts, and that it does not belong in the group of psoriatic disorders.

#### KELOIDS OF THE EARS Presented by DR G D ASTRACHAN

I H, a Negress aged 28, from the West Indies, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. She was first seen on July 2, 1935, at which time she presented numerous enlargements of both ears, the ears being markedly distorted by masses of firm fibrous tissue. These lobulated masses appeared to be firmly attached to the cartilage. They covered the entire posterior surfaces of both ears except a small portion of the lower lobule. The overgrowth of the tissue caused a marked deformity of the helix. There were keloidal scars resulting from a previous surgical excision. The condition had been present for thirteen years.

Operation was performed by Dr J Hoffman of the clinic for patients with tumors. Tissue examined microscopically at the time of operation showed the microscopic picture of keloid. The results shown tonight represent those of the first stage of the operation.

## DISCUSSION

DR J HOFFMAN This patient's ears were pierced when she was a child. Keloids developed at the site of puncture and grew rapidly. The original keloids were excised, but they promptly recurred. During the ensuing sixteen years the patient underwent six operations for the removal of the recurrent keloids. On two occasions she received roentgen treatments, which caused marked reduction in the size of the masses for two years, after that they grew steadily until they were larger than before. When she came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in July 1935 the greater part of the anterior surface and the entire posterior surface of both ears and the adjacent portion of the scalp were involved by bulky masses measuring approximately 7 cm in each diameter. The lesions were the size, shape and consistency of moderate-sized potatoes. After the masses had been excised together with a strip of cartilage 1 cm wide from the outer circumference of the ear there remained the difficult problem of covering the naked cartilage of the anterior and posterior surfaces. The available skin on the anterior surface was freed and slid posteriorly to cover the whole remaining anterior surface. There was no available covering for the posterior surface and for the adjacent postauricular area. The problem was solved by suturing the margin of the ear to the margin of the incision on the scalp thus obliterating the postauricular space.

It was my plan later to dissect the ears free and cover them and the postauricular space by a Thiersch graft over a mold of dental modeling compound.



The patient, however, is pleased with the present result of the first stage of the operation and does not wish to have any further surgical work done to improve its appearance

Seven days after operation each ear received 400 roentgens of radiation, filtered through 1 mm of aluminum. This treatment was repeated three times during the past three months

DR HERMAN GOODMAN Is there any indication that more extensive keloids will not develop?

DR J HOFFMAN In my experience, the best method of treating keloids of this type is by excision and irradiation. The excision is done in such a way as to provide careful, close approximation of the skin with a minimum of trauma. From seven to ten days after the operation the healed incision should receive a single treatment of slightly less than an erythema dose of low voltage roentgen radiation filtered through 1 mm of aluminum. This dose is repeated once or twice at intervals of from two to three weeks. It is essential that intense erythema be avoided. In white patients an objectionable pigmentation may be produced. In Negroes excessive radiation may destroy the pigment cells, bleaching the skin and leaving a conspicuous red scar.

#### LICHEN PLANUS OF THE MOUTH, LICHEN PLANUS ATROPHICUS OF THE SCALP Presented by DR JOSEPH L MORSE.

R A, a woman aged 42, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, says that one year ago she noticed two red spots on the scalp from which the hair began to disappear. There was a smaller lesion on the forehead, which disappeared, leaving a brown stain.

The scalp presents over the right and left temporal regions an oval, sharply demarcated reddish-brown lesion. This area is hairless and atrophic. Close to the hair line on the forehead are several pigmented atrophic macular lesions. On the mucous membranes of both cheeks there are numerous threadlike lesions arranged in a network and having a mildly erythematous base. In the groin is a slightly lichenified, poorly outlined erythematous area.

The Wassermann and Kahn tests and the urinalysis gave negative results. Biopsy of tissue from the scalp and from the buccal mucous membrane showed lichen planus.

#### DISCUSSION

DR MARION B SULZBERGER This case is interesting on account of the unusual localization and the unusual appearance of the lesions of lichen planus on the scalp. I think that any of the members seeing these lesions on the scalp alone and not knowing the histologic picture and not having seen the associated lesions, such as the healed pigmented areas on the forehead and the typical lichen planus in the mouth, would have made a different diagnosis. The lesions on the scalp resemble lupus erythematosus much more closely than they resemble ordinary lichen planus. It is worth noting that lichen planus can do such things on the scalp.

#### A CASE FOR DIAGNOSIS (LYMPHANCITIS?) Presented by DR EUGENE F TRAUB

J V, a man aged 55, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He was presented before the New York Dermatological Society on Oct 26, 1935.

#### DISCUSSION

DR J FRANK FRASER At the meeting of the New York Dermatological Society I expressed the opinion that the disorder was an inflammatory process of infectious origin. It is certainly not a sarcoma arising from fibroblasts. The microscopic picture shows collections of lymphocytes between the collagen fibers pushing these elements apart instead of destroying them.

DR LOUIS TULIPAN I should consider this condition a solid edema following an infection. I think the patient has a lymph stasis around the infected area of

the kind one frequently sees on the face after infections in the nose or in other foci around the face

DR EUGENE F TRAUB This patient's lesion is considerably different tonight from that which he presented when he was first seen. In the center of the lesion there are two healed wounds representing areas where material for biopsy was removed. Two roentgen treatments have reduced the size of the mass materially. The original growth is said to have followed a boil at that site. When the patient was first seen the diagnosis of sarcoid or sarcoma or, as Dr Tulipan suggested, of a low grade infection with edema was considered. A patient with a similar lesion was presented before this section about a year ago, and the majority of the members considered the diagnosis of sarcoid most likely. The condition proved to be true sarcoma, and the patient died. For this reason this possibility should not be overlooked in this case, as it is not easy to make a differential diagnosis.

DR J FRANK FRASER What dose of roentgen radiation has been given, and what has been the effect of the treatment?

DR EUGENE F TRAUB The patient received just a little less than an erythema dose filtered through 3 mm of aluminum, and the lesion has been reduced about two thirds.

#### EPYTHEMA ANNULARE CENTRIFUGUM (DARIER) Presented by DR HENRY D NILES

W T, a man aged 28, born in Poland, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption on the trunk, arms and legs of four months' duration. The eruption began as single small red papules, which gradually enlarged, faded in the centers and formed annular lesions. Smaller annular lesions coalesced to form the large gyrate patches which are now present. The patches have always been dry. At times some of the lesions itch severely. The family history is irrelevant. The patient had never had any cutaneous trouble before the appearance of the present eruption. He has been in this country for the past twelve years.

Scattered over the body, arms and legs are several annular and serpiginous patches of various sizes with slightly raised, dull red, dry, somewhat scaly borders and faintly pigmented but otherwise clear centers. The patches are symmetrically distributed on the arms and legs. One long patch extends from the flexor surface of each wrist to the corresponding axilla.

The Wassermann and Kahn tests of the blood were negative. Microscopic examination and cultures showed no fungi. A biopsy specimen was taken from a lesion on the right forearm. The histologic picture was consistent with the clinical diagnosis of erythema annulare centrifugum. There was no suggestion of psoriasis or tinea.

Since he was first seen on Oct 12, 1935, the patient has received three intravenous injections of calcium gluconate, and calamine lotion has been applied locally, but no improvement has resulted.

#### ERYTHEMA ANNULARE CENTRIFUGUM (DARIER) Presented by DR FRID WISE

O E, a man aged 37, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption on the anterior and lateral surfaces of the feet, the legs and the middle of the thighs, of eleven months' duration. The patient says that on Nov 20, 1934, while working as a fireman, he hit his right leg against the steam boiler. There was a slight abrasion, and a subcutaneous hematoma resulted. Otherwise the history is irrelevant except for a few colds. The eruption began as papules measuring 0.5 cm in diameter, which gradually spread, showing central clearing. These lesions kept on extending until they became large, some of them reaching a length of 20 cm. Several of the lesions coalesced to form gyrate figures. At the beginning the margins were erythematous, raised and firm and were not formed of

individual papular lesions. The patient received roentgen treatments and injections of sodium thiosulfate, which influenced the lesions very little except for the brownish pigmentation and slight scaling. The lesions are slightly pruritic.

Chemical examination of the blood and urinalysis gave negative results. The blood count showed a slight secondary anemia but was otherwise normal.

The biopsy showed perivascularitis.

#### DISCUSSION

DR DAVID L. SATENSTFEN. In Dr. Wise's case the microscopic picture is extraordinary in view of the clinical diagnosis. With this clinical diagnosis one expects to find the usual picture this condition calls for, that is, exudative edema with involvement of the lower portion of the epidermis. Instead of that I found swelling of the walls of the deep vessels, some proliferation of the endothelium and proliferation in the perivascular zone with necrosis. I do not know how to fit vasculitis with the clinical picture. Evidently the patient is suffering from some vascular disease, whether of syphilitic or of tuberculous origin I do not know. That will probably be revealed by further study.

In Dr. Niles' case the picture was that which one expects to find, namely, an exudative superficial edema with some involvement of the under-surface of the epidermis, but there was none of the vesiculation one would expect to find in a fungous infection.

DR. PAUL E. BECHET. The borders of the patches exhibited by Dr. Niles' patient are unusually raised and scaly for erythema centrifugum. The eruption is certainly more suggestive of some fungous condition. The borders on the arm cross each other, and that is suggestive of a creeping eruption. Certainly, these two diagnoses must be eliminated before a diagnosis of erythema centrifugum can be definitely established. Of course Dr. Wise's case is typical from the clinical point of view in spite of the abnormal histologic picture described by Dr. Satenstfen.

DR. ADOLPH ROSTENBERG. I have had the occasion to observe two cases of typical erythema annulare centrifugum of Darier, and I also think that the condition of Dr. Niles' patient does not quite fit the picture of that disorder. In the first place the eruption has a border which is a little too raised, and in some places it appears as though vesicles make up this border. Moreover, in erythema annulare centrifugum of Darier there are circles, but the configuration is not that which this patient presents. The disorder is not a creeping eruption, but it does not agree with the description which Darier gives.

DR. GEORGE M. LEWIS. In Dr. Niles' case an outstanding feature is the symmetry of the eruption, and that speaks against a fungous eruption. An explanation for the symmetry might be that multiple foci of infection are present in the patient's underwear or other clothing. The presence of frank vesicles and pustules along the borders of the configurated lesions is indicative of a fungous eruption. I suggest that repeated examinations for fungi and cultural studies be made. A therapeutic test with the application of tincture of iodine to one area would be valuable. This bizarre eruption lacks many of the features of erythema annulare centrifugum.

DR. FRANK C. COMBES. I do not recall that when Darier first described this condition under the name *erytheme papulo-cucine migrateur* he described an eruption with a crusted border, such as that exhibited by Dr. Niles' patient. Neither did he describe cases in which the lesions were so symmetrically arranged. The condition starts as a papule, which enlarges and flattens, forming a slightly elevated patch. The borders are convex and not concave as in certain areas in this case. The edges of the patch are cordlike, sloping gradually toward the normal tissue and abruptly toward the lesion. This holds true in Dr. Wise's case, but Dr. Niles' case does not remotely suggest this condition to me, in spite of the histologic picture.

DR. MARION B. SULZBERGER. I agree with everything Dr. Lewis and Dr. Combes have just said. I do not think that the condition in Dr. Niles' case is in any way suggestive of Darier's erythema annulare centrifugum. There are

certainly vesicles and pustules on that entire border now, even though the histologic examination did not show them at the time when, and in the area from which, the section was taken. I have observed another case in which I consider the eruption to be clinically identical with that in this one, and in which I was able to find fungi. The suggestion made by Dr. Bechet, that this may be a creeping eruption, may appear plausible at first glance, but when one traces the lesions one finds that they always form a completely closed line. If the disorder is a creeping eruption, the organism causing it has in every instance crept back into its original hole in this case. This is obviously impossible.

DR. HENRI D. NILES. My co-workers and I are much interested in this patient. We considered, of course, the diagnoses which have been mentioned and also that of the serpiginous type of psoriasis. There is nothing in the histologic picture to suggest psoriasis or tinea, as Dr. Satenstein said. The eruption did certainly not correspond to my conception of Darier's disease at the beginning, but in looking up some reports, especially an article by Graham and Throne (*ARCH. DERMAT. & SYPH.* 22:777 [Nov.] 1930), I found that they described lesions of erythema annulare centrifugum with red scaly appearance and also slight pigmentation in the center, as this patient shows. Of course the marked symmetry of the lesions of my patient is unusual. Additional examinations for fungi will be made. I am not entirely satisfied in that respect. As far as larva migrans is concerned, my conception of that disease is that it is mostly limited to Florida and the tropics. This patient has not been any farther south than a few miles south of New York, and he has not been exposed to any infection of that nature. I think that, in spite of the objections to the diagnosis presented, it fits better than any other.

#### A CASE FOR DIAGNOSIS (LYMPHANGITIS) Presented by DR. PAUL GROSS

W. S., a youth aged 16, born in the United States, is presented from the Vanderbilt Clinic. Two months ago, while the patient was in the country, the eruption began with water blisters on the dorsum of the left foot, this was associated with swelling of the ankle. Later the blisters disappeared, but they were followed by red, raised patches which appeared over the entire left leg. These grew larger and broke down, discharging a slight amount of yellow pus. The resulting ulcers healed slowly. The leg and ankle remained swollen and painful.

There are scattered circular lesions, 1 cm. in diameter, covered with crusts and surrounded by areas of purplish discoloration. One of these is discharging serum. The lower half of the leg is indurated and swollen, as is the foot, with pitting edema. The lesions resemble ends of sinus tracts. There is an enlarged, nontender inguinal node in the left groin.

Roentgenograms of the left foot showed normal conditions.

A blood count made on Oct. 9, 1935, shows 100 per cent hemoglobin, 5,020,000 red cells and 9,100 white cells. The differential count showed 62 per cent polymorphonuclear leukocytes, 27 per cent lymphocytes, 3 per cent mononuclears, 3 per cent eosinophils and 5 per cent basophils. The Wassermann reaction of the blood was negative.

The results of cutaneous tests were as follows. A test with old tuberculin in a 1:1,000 dilution produced a slight flare, a test with staphylococcus toxin in a 1:100 dilution produced 2 cm. of erythema, a test with streptococcus toxin in a 1:400 dilution produced an area of erythema 4 cm. in diameter and an elevation of temperature. Cultures and inoculations of animals for sporotrichosis gave negative results.

The biopsy showed scar tissue and chronic inflammation.

#### GRANULOMA ANNULARE (DISSEMINATED) Presented by DR. MARION B. SUZBERGER

C. F., a man aged 29, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of a generalized

eruption of four years' duration. The patient was first seen at the clinic on Sept 24, 1932, because of an eruption of one year's duration. At that time the lesions were annular and were made up of discrete and confluent ivory colored nodules. Tissue was taken from the border of the lesion on the dorsum of the right hand for microscopic examination. The microscopic diagnosis was *granuloma annulare*.

One year later, numerous small lesions developed over the arms. These spread slowly and now cover the entire body. The patient came to the clinic on June 20, 1935, at which time he presented a generalized eruption which was most marked on the forearms, arms and chest. The eruption consisted of numerous discrete and confluent, firm ivory to waxy yellow papules.

At present most of these lesions are grouped in annular arrangement, with a slightly raised, infiltrated border and a depressed center. The large annular lesion on the dorsum of the right hand has almost entirely disappeared as a result of roentgen therapy.

Tests with tuberculin gave negative results in 1:10, 1:100 and 1:1,000 dilutions. The Wassermann, Kahn and Kline tests and examination of the urine gave negative results.

Tissue for microscopic examination was taken from a small lesion over the right scapula, and a diagnosis of *granuloma annulare* was made.

#### DISCUSSION

DR MARION B. SULZBERGER. I think this is certainly an eruption worth showing on account of the unusual picture presented by this *granuloma annulare*. Many of these lesions are small, disseminate and lichenoid papules, giving the impression that one is dealing with an exanthematous eruption. I do not remember ever having seen a case of *granuloma annulare* with such widespread dissemination and with such small, scattered lesions. Nevertheless, I think that one can make the diagnosis from the clinical picture, for there are a few characteristic annular grouped papules in certain areas on the arms. Furthermore, as corroborative evidence that the histologic and clinical diagnosis is correct, one can cite the results of the cutaneous tests with tuberculin. This is a rather characteristic finding in a case of *granuloma annulare*, the patients do not react to tuberculin in spite of the fact that there is evidence of healed lesions in the lungs, as is the case in most inhabitants of cities at the present time. In other words, patients with *granuloma annulare* have a specific anergy to tuberculin. This speaks in favor of the tuberculous nature of the eruption, as discussed in the article on tuberculin by Dr. Wise and me (*M. Clin. North America* 14:1555 [May] 1931).

NAEVUS SYRINGADENOMATOSUS PAPILLIFERUS. Presented by DR. GEORGE M. LEWIS.

M. K., a girl aged 4 years, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of a lesion on the scalp which has been present since birth. On the top of the scalp there is a dime-sized, irregular patch of alopecia. The skin in that area appears atrophic. At one end is a pea-sized, crusted elevation.

A biopsy specimen taken from the elevated lesion shows an intracutaneous epithelial nevus associated with naevus syringadenomatosus papilliferus (Gans). A biopsy specimen taken from the flat part of the lesion shows atrophy.

#### DISCUSSION

DR. GEORGE M. LEWIS. Part of the area represents what may be spontaneous healing. Dr. Sachs may wish to comment on the pathologic observations.

DR. W. SACHS. The picture is exactly the same as the one described in Gans' book. There is cystic dilatation of the sweat ducts, and within the cystic

cavities are little growths. Associated with these growths and with changes in the sweat ducts is an intracutaneous epithelial nevus. There may be some increase in keratosis at the opening of the duct.

DR MARION B SULZBERGER. I think it should be called to the attention of the members who have not seen the patient before that the lesion they now see is not the typical nevus. It is simply a scarred area, which is not characteristic of this type of nevus, in one corner there is a wound showing the site where material for biopsy was removed, obliterating the characteristic part of the lesion. The characteristic part was brownish and had a papillomatous surface.

BOWEN'S DISEASE (PRICKLE CELL EPITHELIOMA) Presented by DR EUGENE F TRAUB

L. P., a woman aged 55, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption in the upper part of the intergluteal cleft of twelve years' duration. A clear history is not obtainable owing to the patient's deficient knowledge of English. Twelve years ago a physician told the patient that she had a crusted lesion, this was treated with roentgen radiation. Five years later she consulted another physician for the same condition. He treated her with sulfur ointment for four years, as well as with cauterization (?).

At the upper margin of the intergluteal cleft there is a lesion measuring 8 cm in diameter. The border presents serpiginous configurations. There are a few adherent crusts, but for the most part the surface is granular and red, with small papillomatous areas. The base of the lesion is moderately indurated. On the right buttock there is a smaller lesion with a pigmented, indurated border. Several histologic examinations made in the past are said to have shown the so-called precancerous dermatosis of Bowen. A recent biopsy showed squamous cell epithelioma.

DISCUSSION

DR EUGENE F TRAUB. There is no doubt as to the correctness of the diagnosis of Bowen's disease in this case. However, because of recent articles in which it was stated that squamous cell epithelioma does not occur in the course of Bowen's disease and because a number of dermatologists believed that this patient was suffering from a squamous cell epithelioma, that point was brought up. It was suggested when this patient was presented at the meeting of the staff of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital that sections be removed from the center of the lesion, which had received roentgen treatments and had been cauterized in some manner. Two such sections were removed, and both showed the presence of squamous cell epithelioma. I believe that Dr Satenstein is of the opinion that squamous cell epithelioma does not occur in an ordinary case of Bowen's disease. This may be true, but in this patient it is probable that the previous treatment may have occasioned such a change.

DR DAVID L SATENSTEIN. My co-workers and I have seen quite a number of patients with Bowen's precancerous dermatosis, and I can remember only one instance in which a neoplasm developed. It took on the cellular characteristics which were noted in the original condition. In the literature, under the name of precancerous dermatosis with development of neoplasms, some cases have been described in which that condition occurred in association with prickle cell epithelioma or with basal cell epithelioma. In a recent article (*Radiology* 25 & [July] 1935) Montgomery discussed that question and concluded that he doubts whether in these cases the original diagnosis was correct, as he and his group believe that Bowen's disease does not degenerate into a malignant condition and that these cases were probably cases of either prickle cell or basal cell epithelioma at the start, with some areas which showed some type of dyskeratosis like that seen in lesions of Bowen's disease. In this case, we found the characteristic

picture of Bowen's disease. At the time the patient was presented at the monthly conference of the members of the staff, I thought that the large ulcerated or eroded area was probably a result of injury or traumatism, I subsequently learned that the patient had received considerable roentgen radiation, I doubted whether any malignant degeneration would be found in the ulcerated area. Pieces of tissue were submitted and examined, and it was difficult to decide whether the lesion consisted of prickle cells or of basal cells, on account of the effects of the irradiation. It was a neoplasm, the type of which could not be determined. As to therapy, my suggestion is that radical excision of the entire affected area be performed and whatever additional therapy is necessary be used afterward.

DR J. G. HOPKINS. I recall a case Dr Fordyce reported under the name of Paget's disease of the buttocks a number of years ago, in which the results of the first biopsies were reported as Paget's disease and the picture looked not unlike that of Bowen's disease. Later biopsies showed epithelioma, some of the sections frankly showed basal cell epithelioma, and some, I believe, prickle cell epithelioma.

DR A. L. CARRION, Puerto Rico. I was much surprised to see this patient here tonight. I saw her about three months ago in San Juan, Puerto Rico. She came to me complaining of the large ulceration on the buttocks and stated that she had received several roentgen treatments. I suspected a malignant condition and ordered a biopsy, which was done at the University Hospital of the School of Tropical Medicine. A diagnosis of Bowen's disease with epitheliomatous degeneration was made. After that I was unable to follow up the patient.

#### LICHEN PLANUS OF THE BUCCAL MUCOSA, PSORIASIS OF THE BODY. Presented by DR. MAX SCHEER.

M. K., a man aged 43, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption of ten years' duration. On the chest, scalp, retro-auricular spaces, extensor surfaces of the legs and glans penis are salmon-colored patches covered with shiny scales. There are also lesions on the fingers and in the nasal folds. The nails are stippled. There is some maceration between the toes. On the mucous membranes of the cheeks are white circinate lesions resembling lichen planus. A biopsy of these lesions shows lichen planus.

#### LICHEN NITIDUS. Presented by DR. ISADORE ROSEN.

D. S., a boy aged 6 years, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, because of an eruption of four and one-half months' duration which is present on the trunk, forehead and legs and is profuse on some of the fingers. There is a linear formation over the right elbow and right side of the chest. There are also lesions on the glans penis. On the front and sides of the trunk are scattered pinpoint and slightly larger shiny skin-colored papules. There is some tendency to grouping. The eruption appeared about one week after the patient received the fifth of a series of injections for protection against whooping cough. At the age of 8 months the patient underwent an operation for empyema. The family history does not indicate the occurrence of tuberculosis.

Tuberculin tests made on Oct. 28, 1935, gave positive results on the right arm in a 1:1,000,000 dilution and on the left arm in a 1:10,000 dilution. A biopsy made on Oct. 14, 1935, showed lichen nitidus.

The patient has received three treatments with ultraviolet radiation from a quartz mercury vapor glow lamp, and slight improvement has resulted.

#### PRICKLE CELL EPITHELIOMA. Presented by DR. MAX SCHIFFR.

J. H., a man aged 58, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of a lesion of

the left buccal mucosa extending to the posterior portion of the pharynx of six months' duration. The patient first noticed sores in the mouth six months ago. There was no pain or discomfort until one month ago. At that time shooting pains occurred, involving the left mandible. The patient applied to the dental clinic for extraction of a tooth to relieve this pain. At present there is a large ulcerated lesion extending from the lower left bicuspid back to the posterior pharyngeal wall and involving the left anterior and posterior pillars and the left tonsil. The borders of the lesion are rolled and are moderately infiltrated. The base of the lesion is covered with a grayish-white membrane. The teeth are markedly carious.

The Wassermann, Kahn and Kline tests were negative. Biopsy showed in the tonsillar region a transitional cell epithelioma resembling lympho-epithelioma, which was highly anaplastic.

#### LUPUS MILIARIS FACIEI DISSEMINATUS Presented by DR. HENRY D. NILES

T. W., a man aged 45, born in the United States, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption on the face of eleven months' duration. The eruption started on the forehead, with groups of small erythematous papules. Since then similar lesions have appeared under the eyes, behind the ears, on the chin, on the cheeks and on the back of the scalp. The lesions appear in groups and on healing leave pigmented, depressed scars. There have been no lesions on the rest of the body, but in the past few months painful deep ulcers have appeared from time to time on the mucosa of the cheeks and lips and on the tongue. These ulcers are preceded by pain, but the patient has noticed no vesicles or nodules. The lesions in the mouth do not leave scars. The patient's general health is excellent. He has not lost weight and has had no cough or night sweats.

Scattered over the forehead, along the anterior hair line, under the eyes, on the chin and cheeks, behind the ears and along the posterior hair line are many round brownish-red nodules the size of the head of a large pin and brown-pigmented atrophic depressed scars. The scars and nodules are most numerous on the forehead. There is a group of larger nodules under the right eye. There is a lentil-sized ulcer, surrounded by redness and induration, on the left side of the mucosa of the lower lip. Pressure with the diascopé reveals apple jelly nodules.

Roentgen examination of the chest revealed no evidence of pulmonary tuberculosis. Tests with tuberculin in 1:1,000,000, 1:100,000, 1:10,000 and 1:5,000 dilutions have given negative results on three occasions; tests with 1:1,000, 1:500 and 1:100 dilutions produced 1 plus, 2 plus and 3 plus reactions, respectively.

Histologic examination of material from a lesion on the forehead and from a lesion on the back of the neck showed many tubercles consisting of giant cells and epithelioid cells, but no caseation, scattered through the cutis.

The Wassermann test of the blood, urinalysis and general medical examination gave negative results.

From May 18, 1935, to the present date the patient has received twenty-four injections of gold sodium thiosulfate. No new lesions have appeared in the past two and one-half months, but there has not been much improvement in the old ones. The possibility of peradenitis mucosa necrotica recurrens was considered for the lesions in the mouth.

#### CHRONIC INFECTIOUS EDEMA OF THE FACE (STEVENS), LICHEN PLANUS HYPER-TROPHICUS OF THE RIGHT LEG Presented by DR. BEATRICE KESTEN

R. S., an American woman aged 58, a housewife, is presented from the Vanderbilt Clinic because of recurrent swellings of the face of forty years' duration and severely itching lesions on the right leg of thirty years' duration.

About forty years ago the patient had erysipelas of the face. Since then she has had recurrent swellings of the chin and of the mucous membranes of the mouth. In addition, intermittent swellings of the nose have occurred in the past



one and one-half years. The latter followed a boil in the nose. A typical attack occurs about every month. It begins with localized swelling of the mouth, nose or chin, the mouth becomes sore, the patient suffers from gastric upsets, she has a temperature varying from 101 to 103 F for two or three days, and she is obliged to remain bedfast for a day or so. The attack lasts from two to three weeks, and during that time some part of the face and usually the mouth become red, sore and swollen. After the attack the skin again appears normal except for the tip of the nose. This remains slightly swollen and dull red. The patient was first seen on Aug 22, 1935. At that time, and again on September 6, she had a typical attack. Since then she has had none except a slight swelling of the tip of the nose on October 28, after she received an injection of staphylococin.

The cutaneous tests gave positive reactions, immediate and delayed, with staphylococin and negative reactions with five different strains of streptococin.

Intracutaneous injections of staphylococin have been given at weekly intervals since September 10.

The history of the lesions on the right leg is as follows. About thirty years ago the patient had an eruption resembling ringworm on the lower extremities for about a year. This cleared up except for about a dozen spots on the right leg. These have slowly grown larger and have been scratched intensely. On the posterior aspect of the middle and inner third from the popliteal area to the middle, of the right leg, there are fourteen rounded and irregular, elevated, well defined plaques in fairly linear arrangement. The lesions vary in size from 1 to 3 by 2 cm, they are brownish and covered with minute horny projections. (A photograph is presented showing the appearance of the lesions on September 6.)

From September 12 to October 21 the patient received six roentgen treatments of 150 roentgens each. Relief from itching and conspicuous regression of the lesions have resulted. About the middle of the right leg, anteriorly, is an isolated elevated nodule about 1.5 cm in diameter. The center is chamois-colored and covered with smooth glistening skin. Surrounding this is a warty collar.

The patient is now in good general health. The diabetes is under control, the urine being free from sugar and the sugar content of the blood amounting to 140 mg per hundred cubic centimeters.

#### DERMATOPHYTOSIS ERYSIPELATOUS DERMATOPHYTID Presented by DR. EUGENE F. TRAUB

J. E., a man aged 34, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption on the left leg of two or three years' duration.

The patient first appeared at the clinic on Aug 12, 1935, presenting erythema with swelling of the lower third of the leg. There were scaling and vesiculation of the toes and of both soles. At that time fungi were recovered from the first toe-nail of the left foot and from the left sole. Tests with trichophyton and oidiomycin gave strongly positive reactions. The test with trichophyton for immediate production of a wheal on the left leg was negative. The patient returned on November 1 with a recurrence of redness and swelling of the left leg. The condition was accompanied by fever and chills. Within three days after treatment consisting of dressings saturated with a solution of boric acid the condition of the left leg was much improved. The patient had several attacks of this kind within the past two years.

#### FAVUS Presented by DR. ANTHONY C. CIPOLLARO

F. D., a woman aged 33, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption on the scalp of thirty-two years' duration. The patient was born in Brooklyn. Her mother, father, two brothers and three sisters, as well as her husband and one child, are free from the disease. The only members of the family affected are the patient and one son. The disease has been present since infancy. It has

been treated with topical remedies, and the patient has been hospitalized for one year, but no improvement has resulted. The area has never been epilated with either roentgen rays or thallium acetate. At present the scalp is for the most part denuded and is scarred and atrophied. There are some active lesions, which are covered with yellowish scales. In places the scales have been removed, leaving brownish exuding surfaces. The skin and nails do not appear to be affected.

LICHEN PLANUS VESICULOSUS Presented by DR HERMANN FERI

E D., a woman aged 36, is presented from the Englewood Hospital, Englewood, N J. Two weeks before the outbreak of her eruption the patient had grip for three or four days. Shortly after she was up and about one of her children was accidentally injured, and the patient had a nervous breakdown which confined her to bed for about two weeks.

When she was first seen there was a vesicular eruption, which was most marked on the neck, chest, flexor surfaces of the forearms, lower portion of the legs and feet, including the soles. In two or three days, heavy desquamation took place, leaving polygonal glistening violaceous papules. The eruption at all times itched intensely. The onset of the eruption was accompanied by fever and malaise sufficient to oblige the patient to remain in bed. During the first three days, while the eruption was vesicular, the patient was given daily treatments with ultra-violet radiation, without any results. On the fourth day, hydrotherapy (prolonged warm baths) and administration of phenobarbital were instituted. After two weeks of this therapy there was marked improvement, the papules had receded almost to the level of the normal skin, and normal pigmentation was being restored.

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## CHICAGO DERMATOLOGICAL SOCIETY

MAX S WIEN, M D, *Secretary*

*Regular Meeting, Oct 16, 1935*

WILLIAM ALLEN PUSEY, M D, *President*

DEEP ULCERATING SYPHILODERM Presented by DR OLIVER S ORMSBY

This man, aged 39, was first presented before this society in December 1925 (ARCH DERMAT & SYPH 14 69 [July] 1926)

At that time the ulceration was extending rapidly in spite of all treatment, and a doubtful prognosis was made by the members present. Dr Harold N Cole suggested that injections of typhoid vaccine be used to supplement the other treatment. This was immediately done, and remarkable results were obtained. Arsphenamine, which had produced practically no effect, was efficient after the injection of typhoid vaccine. While there is marked deformity at present, the disease is apparently under control.

### DISCUSSION

DR WILLIAM ALLEN PUSEY This is an extremely interesting therapeutic result, and I am indebted to Dr Ormsby for calling attention to this method of treatment.

DR OLIVER S ORMSBY The patient is presented because of the therapeutic result. When he was presented ten years ago a number of dermatologists were present, including Professor Dohi, of Japan, and the patient was thought to have resistant syphilis that would prove fatal. The disorder began with nodules on the nose, which ulcerated and progressed rapidly, destroying the nose and a large part of the upper lip. Various methods of treatment were used without effect.

At that meeting Dr Cole suggested that a protein shock be produced with injection of typhoid vaccine. The following day the patient was hospitalized and given such an injection. Within a week the ulceration began to improve, and when the patient was presented two months later the lesions had practically healed. Later other lesions developed, and it took several years before the disease cleared up entirely. The Wassermann reaction has been negative for some time, and the patient is about to undergo a plastic operation. The fact that the patient is alive is due, I think, to the protein therapy. He received only one injection and on the day it was given his temperature rose to 106 F. Treatment with arsphenamine was then resumed, and good results were obtained.

#### LUPUS MILIARIS DISSEMINATUS FACIEI Presented by DR M H EBERT

This man, aged 49, presents an eruption on the face and neck which, he states, appeared about seven months ago. He has always been well. The lesions when first seen consisted of shotty papules from the size of a pinhead to that of a match-head, distributed over the face and involving the eyelids, the alae of the nose and the ears. On pressure with the diascope a brownish macule persisted. There was some diffuse erythema of the face. At present many of the lesions have become absorbed, leaving pitted scars.

The Wassermann reaction was negative. The reaction to an intradermal injection of tuberculin in the form of second-strength purified protein derivative was strongly positive. A roentgenogram showed no evidence of pulmonary tuberculosis.

Biopsy of material from a nodule in an early stage of development on the side of the neck showed multiple foci of round cells throughout the thickness of the corium. At the level of the coil glands there were groups (typical of sarcoid) of epithelioid cells and a few giant cells with a connective tissue capsule. At higher levels lymphocytes, fibroblasts and epithelioid cells were mixed indiscriminately. There was an area of beginning necrosis in the center of the lesion.

The result of weekly injections of neoarsphenamine has been excellent.

#### FOLLICULIS Presented by DR THEODORE CORNBLEET and DR EARL R. PAGE

This boy, aged 4 years, presents an eruption on the extensor surfaces of the extremities. He has been under observation in the hospital for six weeks, but the previous duration of the eruption is not known. He was brought to the hospital because of rheumatic pain, swelling of the wrists and knees and generalized lymphadenopathy.

The eruption consists of follicular papules and nodules in various stages of development. A few lesions on the upper extremities show central necrosis. The lesions leave punctate scarring. During the past forty-eight hours a fresh outbreak of lesions has developed.

On October 9 the Mantoux test showed a marked increase in color. Roentgenograms of the chest revealed no pathologic changes. Examination of the urine showed 1 plus albumin and an occasional hyaline or granular cast. The blood counts were within normal limits. The nonprotein nitrogen content of the blood was 13.5 mg per hundred cubic centimeters. The sugar content was 70 mg. The Kahn reaction was negative. The temperature has not exceeded 100 F rectally, and no increase accompanied the development of the fresh outbreak of lesions.

#### DISCUSSION

DR H E MICHELSON Minneapolis I think that Dr Ebert's patient has lupus miliaris disseminatus faciei. It is interesting to note the many lesions on the scalp. No doubt, in some cases this condition has been diagnosed as acne varioliformis. I am much interested in the mechanism of the formation of these various forms of tuberculosis. One may easily accept the statement that the lesions are the result of hematogenously sown bacteria, but that does not explain why bacteria from an internal focus get into the blood stream and cause lesions only at certain

points or why the lesions take on certain morphologic characteristics. It is doubtful whether the primary polymorphonuclear cells lodge as minute emboli and the reaction takes place about those. Pautrier's experiments and observations on the histologic characteristics of tuberculin reactions show that the inflammation may permeate the vessel from without. At any rate, the entire problem is far from being solved, and the nomenclature at the present time is arbitrary.

I cannot regard the condition in Dr Cornbleet's patient as a papulonecrotic tuberculid. I believe that it is an erythema multiforme-like eruption and that it may be of tuberculous etiology; it is known that the Scandinavian school believes that in children erythema nodosum in all cases and erythema multiforme in some cases are of tuberculous origin.

DR HAMILTON MONTGOMERY. I have discussed briefly the localized and hematogenous forms of cutaneous tuberculosis at recent meetings of the Minnesota Dermatological Society. I can see no reason why, under certain circumstances, tubercle bacilli should not show selective localization in regard to the skin, just as various forms of streptococci show selective localization in regard to different organs of the body, as was demonstrated by Rosenow. The size of the cutaneous lesion as exemplified in either tuberculosis or syphilis depends on the depth of the process and on whether the larger or the smaller and more superficial blood vessels are attacked. Thus, in erythema induratum or in gumma the larger vessels are attacked, whereas in secondary syphiloderm, or in the disorder exhibited by Dr Ormsby's patient—tuberculosis cutis follicularis disseminata (lupus miliaris disseminatus)—the smaller vessels are involved by the organism in question. The condition in Dr Ormsby's patient is a duplicate of that in a patient whom he and I presented a short time ago before this society.

DR CLARK W. FINNERUD. The sections shown by Dr Ebert are interesting in that the changes resemble those of Boeck's sarcoid. However, I am certain that the diagnosis of the presenter is correct.

I did not hear the history in Dr Cornbleet's case, but from the clinical picture my impression is that the condition is a tuberculid.

DR OLIVER S. ORMSBY. The patient of whom Dr Montgomery spoke was expected to be present today, but he failed to appear. He was presented in 1933 (ARCH DERMAT & SYPH 30 137 [July] 1934), at that time he had typical lesions of lupus disseminatus faciei. This case exemplifies clearly the distinction between this condition and sarcoid. There is a close resemblance between the two diseases, especially in Negroes, as has been demonstrated by Dr Nomland. A series of injections of gold sodium thiosulphate completely cleared up the lesions in this patient, and he has remained well for nearly one year.

DR M. H. EBERT. When the patient was first seen there was considerable erythema associated with the eruption, which suggested to some members that the condition might be Lewandowsky's tuberculid, but I think that clinically it fits in the category under which it was presented.

In regard to therapy, I think the patient has shown a good response to neoarsphenamine, which is nonspecific in its action.

DR THEODORF CORNBLEET. Dr Michelson and I are in substantial agreement that the eruption is a tuberculid. I think, however, that it is not of the erythema multiforme type. The lesions are shotty. There are two lesions about the right elbow that are necrotic, and there is a definite scarring left by some lesions that were on the upper extremities. I saw no evidence of scratching which would account for the necrosis. The lesions appear in crops and showers at intervals. The eruption has been present for some time, and unless one is willing to believe that erythema multiforme goes on for a prolonged time, I do not see how that diagnosis can be upheld.

A CASE FOR DIAGNOSIS. Presented by DR. W. W. DUENING, Fort Wayne, Ind.

Mrs. R. S., aged 58, was first seen on July 29, 1935, she stated that she had severely burned her hands with phenol about a year previously, and that the skin

turned white and exfoliated. As healing took place, the patient noticed some irregular black pigmentation in the areas which had come in contact with the phenol. This gradually became more intense, and about three months ago she first noticed some pigmentation of the lips, which followed slight trauma from an ill fitting double denture. Her general health has been good, except for the fact that she had cholecystitis and one attack of jaundice. She lost from 12 to 15 pounds (5.4 to 6.8 Kg) in the past few months.

The eruption involves the thenar eminences of both hands, the vermilion border of the lips and the buccal mucosa. It presents an irregular brownish to blackish hyperpigmentation. In addition, there is some loss of the normal cutaneous markings in the areas involved.

A section is presented, it shows the pigment to be melanin, with many branched cells, giving evidence of pigmentary activity.

#### DISCUSSION

DR S W BECKER. Dr Duemling sent me a small piece of tissue for study, which showed definite pigmentary activity in the form of dendritic melanoblasts. I suggested to him that the burn had produced stimulation of pigmentary activity similar to that found in postinflammatory melanosis. The lesions on the lips are melanotic and are of the type not infrequently seen in dark-complexioned persons, but the patient is not as dark as one would expect for one showing such a reaction. The only pigmentary change resulting from phenol poisoning is ochronosis, which is found mainly in cartilage. I do not believe that the phenol per se had any significance but think rather that the palmar melanosis is a reaction of the type that would follow any burn.

A few weeks after I examined the sections in this case I saw a patient who had a burn involving the wrist and extending onto the palm. The lesion on the wrist had become entirely depigmented, owing to destruction of melanoblasts, and the portion of the burn which was on the palm showed the same type of hyperpigmentation as that exhibited by this patient. This seems to confirm the original impression that it was a burn and not the phenol per se which caused the pigmentation.

DR WILLIAM ALLEN PUSEY. I have been interested in pigmented lesions on the inner surface of the lip for many years. My attention was called to them by a case which I observed thirty years ago and have followed since. I have seen from ten to fifteen cases of this condition, and in all there has been discrete freckling of the lip, though the lesions were not often as dark as those exhibited by this patient. I think they are unquestionably true pigmented lesions of the skin. All the cases except one have occurred in women. In none of the cases has the disorder had any consequences, the condition has not progressed, and as far as I remember, it has not been associated with the formation of similar areas of pigmentation on other parts of the body. I do not associate the lesions with trauma. As to a reason for their occurrence, one must surmise, but it is entirely possible that they may be a senile disturbance, like other senile freckling.

DR W W DUEMLING, Fort Wayne Ind. It was rather hard for me to determine why pigmented lesions should develop on the lip and in the mouth a year after the patient had burned her hand. It seems that if the change in the pigment on the hands is the result of the burn it could not be relieved by electrocautery. I have tried electrocautery, and in some patches the pigment has not returned and the skin looks normal. But I have been using that treatment only a short time, in due time the pigmentation may return.

DR WILLIAM ALLEN PUSEY. In some of my cases the lesions have disappeared temporarily. There is no difficulty in eradicating the lesions on the hands by freezing them for from fifteen to twenty seconds with carbon dioxide snow.

PSEUDOXANTHOMA ELASTICUM Presented by DR RUBEN NOMLAND and DR RALPH H SCULL

This American woman, aged 56, states that her cutaneous trouble has been present for four or five years. Her only complaint is occasional slight soreness about the umbilicus.

There is an eruption about the umbilicus and the inguinal areas, and less marked involvement is present in the antecubital and axillary regions. It consists of a chamois-colored reticulation in the skin, with no elevation or formation of papules except in a restricted area about the umbilicus. There are no angioid streaks of the retina or other abnormalities.

Biopsy revealed the typical course of degeneration of the elastic tissue in the midcutis. The fibers were thickened and curled and assumed an intense blue color with hematoxylin stain. After incineration the structure of the degenerated fibers was still clearcut, probably because of calcium infiltration.

#### DISCUSSION

DR HAMILTON MONTGOMERY This patient, I understand, has no angioid streaks in the retina. This coincides with the experience which my co-workers and I have had at the Mayo Clinic, namely, that not all patients with angioid streaks of the retina have pseudoxanthoma elasticum of the skin. Conversely, in the case of a physician who knew that he had had angioid streaks for several years but said he had not had cutaneous lesions, examination showed a definite picture of pseudoxanthoma elasticum with typical distribution of lesions.

DR M H EBERT I was interested in this case because of the association of the lesions of pseudoxanthoma elasticum with striae cutis distensae, which were numerous and which may indicate a tendency of the elastic tissue to destruction. It was also interesting to note that the location of the lesions of pseudoxanthoma elasticum is quite different from that of the striae.

DR HAMILTON MONTGOMERY The histologic picture of pseudoxanthoma elasticum consists fundamentally of degenerative changes in the elastic tissue of the middle and deeper portions of the cutis manifested by either diffuse or circumscribed nodules. The elastic tissue shows edema and swelling of the elastic fibers and later tinctorial changes, tending to stain bluish with hemosiderin. One patient in the series of eight cases of pseudoxanthoma elasticum which Dr Benedict and I reported (*Am J Ophth* 18 205 [March] 1935) showed lesions confined almost entirely to the belt line. This patient had always worn a tight belt during childhood, hence it appears that trauma may be a contributing factor, as Dr Ebert has just emphasized.

DR M H EBERT I should like to hear Dr Montgomery explain why these lesions have the peculiar yellow color, whereas other striae are white.

DR HAMILTON MONTGOMERY The yellow color of the lesions is probably explainable by the peculiar degeneration of the elastic fibers together with the normal border zone between these degenerating fibers and the epidermis, resulting in a peculiar type of coloring reaction comparable to that which takes place in a blue nevus of Jadassohn, the lesion appearing blue though the cells of the nevus are laden with melanin and not with hemosiderin.

DR RUBEN NOMLAND I think this case is interesting because it shows that pseudoxanthoma elasticum is not necessarily associated with angioid streaks of the retina. I am glad that Dr Montgomery mentioned the dark blue staining of the degenerated elastic fibers with hematoxylin because this led me to believe that the appearance is due to deposits of calcium in the fibers. I have incinerated many specimens and found on the slide a heavy white deposit of what I believe was calcium, this was many times greater than that left when normal skin is incinerated. My co-workers and I intend to carry out our investigations further and to prove, if possible, that there actually is an increased amount of calcium in the tissue.

## LYMPHANGIOMA CIRCUMSCRIPTUM Presented by DR F E SENEAR and DR MINNIE O PERLSTEIN

This boy, aged 9 years, is said to have had a reddish "birthmark" in the left patellar region at birth. About three years ago this lesion began to extend peripherally, it became elevated and has gradually developed until at present a palm-sized papillomatous mass is evident under the left patellar region. The lesion bleeds freely on slight trauma.

## DISCUSSION

DR WILLIAM ALLEN PUSEY I prefer to call a condition like this simply lymphangioma, it is a congenital lymphatic tumor, a lymphatic nevus.

DR F E SENEAR I do not understand clearly what Dr Pusey's point is. Some of these lesions are not present at birth but appear early. Some apparently develop as the result of stasis in the blood vessels or lymphatics. This lesion at birth was apparently not of the present type. It is known that the verrucous type of lesion develops from the small grapelike clusters, but in this case there is a reddish color which indicates that the lymphangiomatous element may have developed on a basis of venous stasis.

DR WILLIAM ALLEN PUSEY My conception is that a nevus is any congenital tumor of the tissues, it may consist of any body tissue. I have under observation now a child with a lesion of the tongue which is a mixed hemangioma and lymphangioma.

DR H E MICHELSON, Minneapolis This type of lesion does not respond to radiation therapy. Surgical or destructive treatment is advisable.

## LYMPHOSARCOMA WITH MIKULICZ' SYNDROME Presented by DR THEODORE CORNBLEET and DR EARL R PAGE

This Negro boy, aged 7 years, presents bilateral swellings of the parotid glands, which his mother first noted about three months ago. The glands gradually enlarged, and somewhat later the mother noted enlargement of the abdomen. About one month ago tissue from a supraclavicular lymph gland was removed for examination at St Luke's Hospital, and a diagnosis of lymphosarcoma was made.

At present the patient exhibits the gross enlargement of the salivary and lacrimal glands which constitutes the Mikulicz syndrome. The parotid tumors are of about equal size, hard and not attached to the skin. The other salivary glands and the lacrimal glands are likewise hard and enlarged. There is generalized lymphadenopathy, the spleen and liver are moderately enlarged and both seem hard and somewhat nodular.

The leukocyte count averaged about 6,000, the differential count was normal.

No direct cutaneous manifestations are evident, but the patient is presented because of the great rarity of the condition and its relationship to the lympho blastomas.

## A CASE FOR DIAGNOSIS (SPIEGLER-FENDT'S SARCOID?) Presented by DR M H EBERT

This woman, aged 47, was first seen four months ago with a nodule on her right forearm, which, she stated, appeared spontaneously about three months previously. The lesion was a brownish-red oval plaque, firm to the touch, it measured 1.5 by 2 cm and was elevated approximately 5 mm. A small piece was excised from the edge for microscopic study. Since that time the tumor has disappeared spontaneously, leaving a reddish scar.

Histologic examination showed that the tumor was poorly circumscribed. It occupied the entire corium with the exception of a narrow zone under the epidermis. It was made up of round cells which had largely replaced the normal collagen. The mass was supplied with many newly formed capillaries. The cells consisted of fibroblasts, reticulocytes, a few plasma cells and a large number of cells.

apparently of the lymphocyte type. These cells had a narrow zone of cytoplasm and a hyperchromatic nucleus. Mitotic figures were noted in the larger cells, and an occasional giant cell was seen.

## DISCUSSION

DR CLARK W FINNERLUD. It seems to me that the symptoms in this case agree with all that is known about one type of Spiegler-Fendt's sarcoid. Histologically it is difficult to determine whether it is a purely inflammatory process or whether it is sarcoma largely of round cell type. The fact that the lesion disappeared spontaneously agrees with the diagnosis.

DR H E MICHELSON, Minneapolis. My experience with Spiegler-Fendt's sarcoid is limited to one case which was reported by Dr Sweitzer and, I think, accepted as an authentic example. The microscopic picture in that case was entirely different from that in Dr Ebert's case. In the case reported by Dr Sweitzer diagnosis of sarcoma had been made, but the cells were not penetrating as in a true sarcoma.

DR M H EBERT. I think that Spiegler-Fendt's sarcoma is a poor term. Ganz says that there is no such entity, he is of the opinion that conditions classified as Spiegler-Fendt's sarcoma either belong to the lymphoblastoma group or are infectious granulomas. Lewis made the distinction between the generalized type of Spiegler-Fendt's sarcoid and the isolated type. The generalized lesions correspond entirely to those to which Dr Michelson referred, but clinically the isolated lesions mentioned by Lewis were exactly like the one exhibited by the patient presented. Clinically those lesions are not malignant. They respond to administration of arsenic and at times disappear without medication. There are a few plasma cells. The disorder may not be an entity at all and is perhaps a reaction of the reticulo-endothelial system to some irritant.

XANTHOMATOSIS (GENERALIZED). Presented by DR MAX S WIEN and DR MINNIE O PERLSTEIN.

W O, a Polish man aged 43, presents an asymptomatic eruption of two months' duration. He states that it first appeared on the wrist and forearm and rapidly became generalized to its present extent without variation. His general health has always been good except for the fact that he sustained a severe blow to the abdomen eight years ago. Immediately after this injury the abdomen began to enlarge. The patient states that he suffered from polydipsia and polyuria for eight or ten years but experienced no change in appetite. General physical examination gave essentially negative results except for the cutaneous eruption.

The eruption is diffusely scattered over the entire body, except the face, palms and soles, the skin at the joints is particularly involved. The essential lesions consist of discrete acuminate, shotty erythematous papules from the size of a pinpoint to that of a match-head. The intervening skin is unchanged. The apex of the lesion is yellowish white, but no exudate can be expressed. The lesions do not disappear on pressure. There is no confluency of lesions, but the older ones increase in size, varying in shape from round to linear. In addition multiple subcutaneous lipomas are scattered over the abdomen and back. The eyelids and the mucous membranes are not involved.

The Wassermann reaction was negative. Examination of the blood gave essentially normal results in regard to erythrocytes, leukocytes and differential count, the sugar content was 187 mg per hundred cubic centimeters, the cholesterol content, 410 mg, and the urea nitrogen content, 16.35 mg. When the specimen of blood was permitted to settle it had a heavy lipoidal serum. Urinalysis revealed albumin but no sugar.

Histologic examination showed that the epidermis was unchanged. In the corium were many nodules composed of large cells with granular cytoplasm and small from oval to round nuclei. The cells were arranged in solid groups and



were separated by a loose fibrillar stroma. There was no evidence of inflammation, the sudan stain showed that the cytoplasm of the cells was filled with lipoid, and in the stroma there were also heavy deposits of a homogeneous sudanophilic material.

## DISCUSSION

DR CLARK W. FINNERUD: I think this case is an instance of xanthoma diabeticorum. Several years ago (*ARCH. DERMAT. SYPH.* 3:692 [May] 1921) Dr Ormsby presented a patient with a similar clinical picture, except for marked involvement of the palms. At times the urine contained sugar, but often it did not. The sugar content of the blood is high in Dr Wien's patient, amounting to 187 mg per hundred cubic centimeters. Xanthoma diabeticorum is known to occur without the presence of sugar in the urine. The patient whom Dr Ormsby presented received a strict antidiabetic diet, and the eruption disappeared. He had recurrences on several occasions when he lived chiefly on liquor and sweets.

DR WILLIAM ALLEN PUSEY: This case interests me, for the condition is an almost perfect reproduction of one that I observed nearly forty years ago. The patient was a saloon-keeper, and he also had numerous lipomas. He had sugar in the urine, but he lived for many years. At about the same time I treated a child with extensive xanthomatosis who had marked nondiabetic polyuria. There was a large xanthoma in the cornea, and the boy nearly died from xanthoma of the larynx before a tracheal tube was inserted. How frequent are the cases in which sugar is not present? As I recall, xanthoma with polyuria alone was rare when I looked up the literature, and I have seen no case other than the one to which I referred.

DR H. R. FOERSTER, Milwaukee: This patient's blood has a high cholesterol content, and it is my impression that the cholesteremia is the main factor in the causation of the disease and that the diabetes is secondary. I observed a similar case recently in which examination of the blood showed a high cholesterol content, a relatively normal sugar content and absence of glycosuria, in that case also the lesions disappeared after the patient had followed a fat-free diet.

DR HAMILTON MONTGOMERY: I recently saw two patients presenting lesions similar in size and extent to those exhibited by Dr Wien's patient, in both of those patients the lesions were found in the trachea and interfered with speech. Both of the patients showed evidence of diabetes insipidus but no disturbance of the chemical composition of the blood in regard to lipoids. I have also seen two other patients with similar small generalized xanthomatous lesions who had a marked increase of all the lipid components of the blood, the total content of lipids being about four times the normal. I do not think that there is a clinical picture diagnostic of xanthoma diabeticorum, but I believe that these small types of lesions may be common to various forms of cutaneous xanthomatosis.

## PRIMARY AMYLOIDOSIS OF THE SKIN Presented by DR T. K. LAWLESS

This man, aged 65, of Persian descent, complains of a pruritic eruption on the lower portions of both legs, the disorder has been present for twenty-three years. The individual lesions are papular and nodular, and some appear in plaque formation. They vary in color from that of normal skin to brownish red and are markedly elevated and definitely circumscribed. Most of the lesions are capped by thin scales. There is no definite arrangement, although many are perifollicular. The condition has been slowly progressive, and the surrounding skin has become markedly hyperpigmented. The eruption is complicated by a moderate grade of varicosity.

The blood pressure was 160 systolic and 90 diastolic. The blood count was normal. The Wassermann reaction was negative. The urine showed a negative reaction for the Bence-Jones protein.

The results of a biopsy were as follows: The epidermis showed marked hyperkeratosis, acanthosis and parakeratosis and intracellular edema.

The interpapillary pegs were elongated. The corium showed subdermal vesicles and marked increase in fibrosis. The cellular infiltrate was perivascular and predominantly lymphoid in character. The tissues were edematous. The striking feature was the appearance of large areas of tissue reacting specifically to special stains for amyloid.

## DISCUSSION

DR RUBEN NOMLAND. Though localized amyloidosis is a rare disease, it seems to present an extremely consistent picture in the majority of cases. Dr Lawless' patient has an involvement practically identical with that exhibited by the patient whom I presented two years ago (*ARCH DERMAT & SYPH* 29 470 [March] 1934). There are several interesting features about the disorder, especially when it involves the legs. I think that in all cases of chronic pruritic eruptions of the legs the diagnosis of localized amyloidosis should be considered. The fact that this case is far advanced brings me to the discussion of the elementary lesion in local amyloidosis. In reading the textbooks and foreign articles one receives the impression that the lesion is translucent, resembling a vesicle. I think this is wrong in most cases. The earliest lesion is brownish and small, not much larger than a pinhead, and as it grows larger it may appear like some of the special varieties of lichen planus or perhaps like ordinary lichen planus. The amyloid is deposited in the subpapillary layer of the cutis, and I think that the sections Dr Lawless presents prove the contention I made several months ago, namely, that the amyloid is deposited in cells and is not an infiltration into tissue spaces.

Dr Lawless told me he made the injection of congo red, this has proved successful in several cases of which I know, but I cannot see any evidence of the local reaction of congo red in this case. I believe the amyloid appears in cells about the vessels, but whether it is analogous to the infiltration of cells by the xanthomatous substance I do not know. I think it is probably picked up from the circulating blood by the cell.

DR H E MICHELSON, Minneapolis. The question of the pathogenesis of amyloidosis is not settled. It is difficult to know why or how the amyloid is formed. Amyloidosis can easily be produced in experimental animals by repeated injections of bacteria or other substances. This purely localized type may not be closely related to the more systemic types and may be only a secondary manifestation of chronic irritation. I should question the rationale of fever or roentgen therapy.

DR T K LAWLESS. The injection of congo red was given two months ago, and the effect has probably disappeared.

My co-workers and I believe that this condition may be connected with injury to a nerve, and we are studying the nerve endings in cases of primary amyloidosis of the skin. The patient is presented specially to demonstrate the effect of therapy. The lesions on the left leg are much flatter and softer, and this is due to the fact that the man has received nine treatments with hyperpyrexia at intervals of a week.

DR RUBEN NOMLAND. In the two cases I have observed the more severe disorder improved about 75 per cent, and the one of more recent origin improved approximately 90 per cent as a result of moderate doses of roentgen therapy, the course consisting of not over six treatments in doses of  $\frac{1}{2}$  unit (160 roentgens). The response was almost the same as in cases of lichen simplex chronicus.

DR F E SENEAR. Several years ago Dr Lieberthal described the shin-guard type of lichen planus, and when Dr Lawless' patient was presented Dr Michelson and I remarked that his disorder resembled that described by Dr Lieberthal (*J Cutan Dis* 33 395, 1915). I asked Dr Lieberthal about it, and he states that this case is similar to the one he described. He says that the histologic picture is different, but I agree with what Dr Nomland said about amyloidosis and with his statement that probably in the past in many of the cases the disease has been mistakenly diagnosed as hypertrophic type of lichen planus.

DR DAVID LIEBERTHAL. This case is similar to one I presented before the American Dermatological Association and reported in 1915. The clinical and

histologic pictures, however, did not correspond to those in Dr Lawless' case I may add that in my case the administration of arsenic effected a cure within a reasonable length of time Dr Nomland's remarks regarding amyloid deposits are well taken

DR WILLIAM ALLEN PUSEY This patient presents the syndrome which used to be called lichen planus obtusus In my textbook there are illustrations showing the lesions That those lesions are due to amyloid degeneration clears up another point of dermatology Has Dr Nomland ever tried the same staining methods on lichen planus?

DR RUBEN NOMLAND Yes, but without effect

HEMOCHROMATOSIS Presented by DR CLARK W FINNERUD and DR RUBEN NOMLAND

This man, aged 48, came to the medical clinic because of vague discomfort in the back and stated that his skin had become darker during the past two or three years

The darkening of the skin is most marked on the face, arms and legs The liver is palpable 4 fingerbreadths below the costal margin, and there is a mild secondary anemia

The sugar content of the blood varied between 104 and 164 mg per hundred cubic centimeters, and there were traces of sugar in the urine while the patient was following a diet with a dextrose content of 400 Gm

A section and staining of tissue with potassium ferrocyanide showed deposits of hemosiderin in cells about all the sweat glands and to a slight extent about all the blood vessels There was an increased amount of melanin in the basal cell layer and in the layers above it in the epidermis

#### DISCUSSION

DR HAMILTON MONTGOMERY My co-workers and I see a few patients with hemochromatosis at the clinic every year because the internists are on the lookout for any pigmentary disturbances in the skin and send the patients to us to take specimens of the skin for biopsy In one case I observed some time ago the question of Addison's disease had been raised because the patient had a low blood pressure and because the bluish hue of the skin was masked by increased melanin pigmentation However, a biopsy showed definite deposits of hemosiderin I wish to emphasize that pigmentation due to any of the heavy metals, whether iron, as in hemochromatosis, silver, as in argyria, or arsenic, mercury, etc, may in certain persons have a stimulating effect on basal and dendritic cells in the epidermis, thus causing an increase in melanin pigment, which when due to mercury, iron or silver may tend to mask the other characteristic hue of pigmentation caused by these metals The section in Dr Finnerud's case of hemochromatosis also illustrates the role that the reticulo-endothelial system plays in the skin in some patients with this condition The hemosiderin is deposited not only about the substantia propria of the sweat glands but in endothelial cells of the capillaries and interchanged between these and dendritic cells of the epidermis When the dendritic or basal cells of the epidermis take up the hemosiderin they seem to lose their ability to form melanin

PUSTULAR PSORIASIS (RECALCITRANT ERUPTION OF THE PALMS AND SOLES) Presented by DR M H EBERT

This patient, a salesman aged 36 presents an eruption on the palms and soles which was first noted two years ago as groups of "white blisters" on the arch of each foot These lesions dried up, scaled off and recurred continuously About nine months ago similar lesions appeared on the palms and scaling patches were noted below the elbows The patient has been under observation for six months

When he was first seen he presented dry, keratotic, scaling patches on the center of each palm and on each thenar eminence. Pinhead-sized whitish intra-dermal pustules appeared in groups from time to time in these patches. Similar lesions were present on the plantar arch and the lateral surface of each foot. There was a hyperkeratotic, scaling plaque below each elbow which seemed somewhat thinner and less well defined than the plaques of ordinary psoriasis. Vesicles or pustules never appeared in the patches on the elbows. The scalp was clear. During the period of observation the plaques on the elbows disappeared, but the other lesions persisted. At present there are keratotic patches in which a few pustules appear occasionally and slight pitting of the nails.

Specimens for biopsy were taken, including two flat-topped white pustules in an early stage of development at the base of the left palm.

Histologic examination revealed considerable hyperkeratosis and acanthosis and a few areas of parakeratosis but no elongation of the papillae. The stratum granulosum was well preserved. Vesicles and pustules in various stages of evolution were seen in serial sections. The smallest began as microscopic vesicles in areas of marked intercellular and intracellular edema. These were filled with serum and occupied the space of a few rete cells. The largest covered several papillae. Some were filled with serum containing a few leukocytes, while others were packed with polymorphonuclears. The roof was the stratum corneum, and the floor consisted of a few layers of edematous cells through which many leukocytes were migrating. There was some round cell infiltration about the vessels of the upper layers of the corium.

#### DISCUSSION

DR E. A. OLIVER. This condition, I believe, belongs in the group described by Andrews and his co-workers as recalcitrant eruptions of the palms and soles (*ARCH. DERMAT. & SYPH.* 29:548 [April] 1934). During the past year I have had under my care a young man suffering from a deep-seated vesicular eruption of both palms and soles. He had consulted several competent dermatologists who had treated him for epidermatophytosis. After several examinations for the fungus had given negative results, a careful search was made for foci of infection. After four devitalized teeth were extracted, a great deal of improvement occurred, the hands and feet became almost free from lesions. At about the same time a psoriasis-like eruption appeared over the arms, chest and upper portion of the back. The finger-nails also took on a psoriasis-like appearance. Search was continued for more foci of infection, and prostatic massage yielded considerable pus, only after repeated prostatic massage did the lesions on the hands and feet completely clear up. The psoriasis-like eruption disappeared from the body, but the finger-nails still appear to be affected with psoriasis. The palms and soles have been entirely clear for the past nine months.

DR JAMES H. MITCHELL. My experience has been similar to that of Dr. Oliver. After I had read Dr. Andrews' article two patients came under my observation. One had an infection of the tonsils, teeth and prostate. As a result of excision, extraction and massage the lesions cleared up. The other man had infected teeth and tonsils, and after these foci were removed his lesions cleared up. The patient I presented before this society is still under observation. She still has some lesions of the palms and soles, but the lesions are more pustular, although the scaling areas on the heels and soles are almost identical with the lesions exhibited by Dr. Ebert's patient. The lesions on the palms are small vesicles which later become pustules. The histologic picture seems to be identical with that in Dr. Ebert's case.

DR H. R. FOERSTER, Milwaukee. In this case I should hesitate to accept a diagnosis of pustular psoriasis based on the appearance of the palmar lesions alone because of the absence of typical clinical lesions of psoriasis. The dry, scaly patches on the extensor surfaces of the forearms and elbows I consider not psoriasiform but ichthyotic. The absence of demonstrable organisms and the resistance to fungicides, point to the diagnosis of acrodermatitis continua.

DR M H EBERT The presentation of patients with this type of disorder at meetings of the dermatologic societies in New York seems to be the signal for heated discussions. There are apparently two schools. One classifies all such disorders as pustular psoriasis and lets it go at that, and another, that of Andrews and his followers, designates them as recalcitrant eruptions of the palms and soles but expresses no conviction that the disorder is psoriasis. In this case and in several others in Dr Ormsby's practice repeated search for fungi was made and none were found. The histologic picture fits exactly with that of the 'ids' associated with active dermatophytosis on the feet when there are lesions on the palms. Some of the dermatologists in New York agree with Andrews that there is a focus of infection which produces this type of eruption on the soles. This patient presents an eruption on the palms and some involvement of the nails. I think that the discussion centers about the same condition, but whether it is pustular psoriasis, I think, has not been determined and cannot be determined pathologically any more than clinically.

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## BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M D, *Secretary*

*Oct 24, 1935*

EUGENE F KELLEY, M D, *President*

AINHUM Presented by DR ADOLPH ROSTENBERG

This Negress, aged 71, born in South Carolina, has resided in New York for the last thirty-five years and has never been out of the United States. She says that as far as she knows there has never been a similar trouble in the family. Her past history is irrelevant, and she cannot remember ever having injured the affected toe.

The patient states that about four years ago she occasionally had pain between the fourth and the fifth toe of the left foot and that in the last two years the pain has become more severe. Since August 1933 she attended a "foot clinic" but obtained little relief. She first noticed a ring at the base of the toe in April or May 1933. At that time the pain became so intolerable that she could not wear a shoe or even a stocking.

The patient first came to the clinic of the Sydenham Hospital in June 1935. At that time examination revealed a hard fibrotic band situated almost at the proximal end of the fifth toe of the left foot. This band encircled the toe and compressed it to such a degree that the portion of the toe distal to the band appeared bulbous. At present the toe is extremely tender to touch and painful on motion, it does not appear to be red or inflamed. The roentgen examination of the toe gave negative results.

Treatment has consisted of administration of 5 drops of a saturated solution of potassium iodide three times a day and of ten intravenous injections of a 10 per cent solution of sodium iodide at biweekly intervals. On this regimen rapid improvement occurred, for the past two months the patient has been able to wear shoes, and she can touch and move the toe without experiencing pain or discomfort.

### DISCUSSION

DR RAPHAEL BREAKSTONE Most of the cases of ainhum reported occur in Negroes in the tropics. In this case the constriction is not marked and the fibrotic band is not pronounced. I do not believe that the medication applied has caused absorption of the band. For these reasons I do not think that this is a case of ainhum.

DR DAVID BLOOM I believe that the relief from pain is not due to the medication but, on the contrary, was caused by the cessation of the excessive treatment which the patient received regularly in clinics. In the case which Dr Newman and I reported a few years ago (*ARCH DERMAT & SYPH* **27** 783 [May] 1933) there was also considerable pain in the little toe. This could not be relieved by baths of potassium permanganate or by the application of boric acid ointment.

The patient presents ainhum as typical as that which one finds described in the literature, except that the roentgenogram does not show any absorption or destruction of bone. I believe that that will develop as the condition progresses. It should be stressed that in the case which Dr Newman and I reported there was a history of injury to a corn. I cannot help believing that ainhum is due to an injury in a person inclined to react with local fibrosis.

DR PAUL GROSS I think it quite possible that the condition is an early phase of ainhum, and although the constriction was not visible a definite sclerosing band was felt on palpation. The relief from pain resulting from administration of potassium iodide is purely symptomatic.

DR ADOLPH ROSTENBERG I agree with the remarks of Dr Bloom and Dr Gross. The effect of potassium iodide is, no doubt, symptomatic.

#### PUSTULAR PSORIASIS Presented by DR ADOLPH ROSTENBERG

A L, a woman aged 47, presents an eruption of nine months' duration. She suffered frequently from attacks of tonsillitis and peritonsillar abscess. In January 1935 she submitted to a tonsillectomy. The present cutaneous condition began with swelling of the right toe and discoloration of the nail. The other toes and fingers soon became similarly involved. At the time of the onset of the eruption bursitis of the right knee developed, this was punctured and drained.

When the patient was first seen, about two months ago, she presented typical psoriatic lesions on the elbows, forearms and lower extremities. Several nails of the toes were missing, and the end-phalanges of the toes and fingers were enlarged and covered with a soft crust. On pressure a gumlike purulent material could be expressed. Examination of that material for fungi as well as examination of the blood and urine gave negative results. Improvement has resulted from roentgen treatment and from the application of a weak ointment of anthralin (di-hydroxyanthranol).

#### DISCUSSION

DR DAVID BLOOM Essentially there is no difference between the various types of psoriasis, except in the degree of exudation. The name pustular psoriasis is given to the clinical type of psoriasis which is associated with tiny pustules and which is mostly confined to the palms and soles. This patient has no pustules. The changes in and around the nails are seen in psoriasis characterized by increased exudation. I should diagnose the condition as psoriasis of the exudative type. Histologically one finds in exudative psoriasis more edema and more exudation of cellular elements. This is represented clinically by crusted lesions.

DR DAVID L SATENSTEIN The concept of psoriasis is constantly changing. At present dermatologists include in this class conditions which twenty or thirty years ago would have been regarded as entirely foreign to this entity. The patient at present has a pyogenic paronychia which is responding slowly to therapy. Psoriatic lesions on certain parts of the body do not necessarily exclude a second dermatosis. Whether this paronychia is psoriatic or not cannot be determined at present. Only the clinical course of the disorder will establish that diagnosis.

DR ADOLPH ROSTENBERG In my opinion none of the patients recently presented at various meetings has exhibited as convincing proof of the clinical entity of pustular psoriasis. I cannot see how one can consider my case one of psoriasis and multiple paronychia.

#### ARSENICAL KERATOSIS AND EPITHELIOMA Presented by DR DAVID BLOOM

Mrs C C aged 49 born in Ireland was presented before the New York Dermatological Society on Oct 22 1935 by Dr Edward R Maloney.

## DISCUSSION

DR. LEO SPIEGEL. An interesting feature in this case is the presence of lesions on the palms and soles. Dr. Fox called my attention to the fact that in arsenical keratosis the lesions usually occur on the outer border of the palms and soles. I am therefore of the opinion that the eruption is not due to arsenic.

DR. F. E. CROSS. Most of the members have observed cases of similar eruptions. The lesson to be learned is one of prophylaxis. If every physician when prescribing arsenic wrote *non icipetatur* on the prescription, the patient would be spared the sequelae due to ingestion of arsenic.

DR. DAVID SATENSTEIN. I have seen patients with keratoses all over the palms and soles and sometimes on other parts of the body. Comparatively few of the lesions become malignant. In reply to Dr. Cross' suggestion, it may be stated that one cannot prevent patients from going from one clinic to another. That is their privilege. One should warn patients and tell them the amount of medication that they receive, if that is not done serious complications may result.

DR. MARION B. SULZBERGER. It appears that this patient is the exception, because thousands of patients are receiving arsenic and in only a few do arsenical keratoses develop. Apparently when this condition develops an idiosyncrasy or susceptibility to arsenic, perhaps a predisposing localized abnormality in his skin, is present. I have considered the possibility that this predisposing factor may be a sharply demarcated, local epithelial sensitivity to arsenic, analogous to that found in patients with contact dermatitis. I have tried patch tests on such patients, but I have obtained no conclusive results as yet. It is interesting to note that Michael Ebert and others have shown that intradermal injections of minute quantities of arsphenamine do in a few instances produce precancerosis after an interval of several months while in other cases like injections produce practically no change.

DR. ARTHUR SAYER. The question to be determined in this case is whether the keratoses are purely arsenical or whether some keratosis developed as a result of the roentgen ray treatments which the patient received. Possibly a combination of these factors is the responsible cause of the keratoses.

DR. DAVID BLOOM. Unfortunately the superficial epithelioma on the patient's back was treated in the radiotherapy department before my co-workers and I had a chance to examine it microscopically. The patient did not receive roentgen therapy for the psoriasis before the epitheliomas developed. I did not elicit any history indicating that cutaneous or other malignant disease has been observed in the patient's family. I am inclined to think that the superficial epitheliomas as well as the squamous cell epitheliomas were produced by the ingested arsenic and were not due to coincidence. This patient has no pigmentary disturbance.

## KRAUROSIS VULVAE. Presented by DR. ADOLPH ROSTENBERG

This patient, aged 67, has an irrelevant past and family history. She presents a disorder of eight years' duration, limited to the vulva and inguinal region. There is definite atrophy of the labia majora and minora pudendi, and the clitoris is absent, the introitus is markedly narrowed, and any manipulation causes pain.

On the site of the labia minora pudendi there are two adjacent, slightly protuberant firm, reddish lesions the size of an almond. One lesion was removed by electrodesiccation. The patient is receiving roentgen treatment.

## DISCUSSION

DR. THEODORE ROSENTHAL. I agree with the diagnosis, but confirmation based on histologic examination appears desirable. Therapy is the primary consideration in this case and I think that a total vulvectomy is indicated.

DR. DAVID L. SATENSTEIN. Kraurosis vulvae in its later stages is always characterized by sclerosis and atrophy. Malignant neoplasms may and often do develop at this stage. In this case the tissues are soft, grayish white, slightly infiltrated and mostly confined to the vaginal mucosa. I believe that the disorder is a leuko-

plakia which is degenerating into a malignant neoplasm. The best therapy is a combination of surgical intervention and irradiation.

DR SAMUEL FELDMAN. I agree with Dr Satenstein. There is little kraurosis to be seen. There is only one small area at the fourchet, where the skin is glossy and thin and shows denudation of the epithelium in the center. The rest of the skin of the vulva is thickened, opaque and gray. The tumors are located in the areas of leukoplakia.

DR ADOLPH ROSTENBERG. In the diagnosis of kraurosis vulvae one must consider the stage of the disorder. One finds complete atrophy only in the end-stage. In this case the disorder has not progressed that far, and therefore only partial atrophy is present. The clitoris, for instance, and the labia minora pudendi have entirely disappeared. The presence of pronounced leukoplakia, the shrinking of the introitus vaginae and the presence of carcinomatous transformation establish the diagnosis of kraurosis vulvae.

ACNE CONGLOBATA. Presented by DR VAN ALSTYNE H. CORNELL.

C. K., a boy aged 15, came to the Metropolitan Hospital in June 1935, because of an eruption of three months' duration. The patient presents on the face, on the upper part of the chest and back and on the posterior aspect of the neck numerous elevated, puffy, vegetating lesions. Many scars are scattered throughout the aforementioned regions.

The Wassermann test was negative. The chemical examination of the blood gave normal results. No bromides were found in the urine on several occasions. The basal metabolic rate was -13 per cent. The condition of the patient improved after he received ten roentgen treatments.

#### DISCUSSION

DR MAX BERKOVSKY. I believe that in addition to roentgen irradiation the treatment should include injections of foreign protein, such as milk.

DR THEODORE ROSENTHAL. I agree with Dr Berkovsky as to the general type of treatment, my co-workers and I have used a 3 per cent aqueous solution of phenol intramuscularly with good results, particularly in this type of patient.

DR DAVID L. SATENSTEIN. The patient presents a rather mild type of the disease. The process is essentially one of breaking down of the tissues, due in part to liquefaction of the pathologic exudate as well as of the affected tissues. These areas are replaced by granulation tissue resulting in scar formation. These scars, in the course of time, gradually atrophy. Infection apparently plays little part in the process. There is no specific therapy, foreign proteins of various kinds, vaccines, roentgen radiation and various local agents are used, but none of them is specific. The building up of the patient's general condition is the important part of the treatment.

DR ISIDORE M. LASHINSKY. This patient is between 15 and 16 years of age. The use of roentgen radiation in treating acne in patients under 18 years of age has been deprecated, rightly, I believe. My co-workers and I have obtained fairly good results by injecting a 65 per cent dilution of alcohol into sebaceous cysts and cystic acne. We have found that the alcohol liquefies the sebaceous matter and eventually, after a few injections, destroys the capsule. We thus avoid using the scalpel.

DR DAVID BLOOM. I have treated a number of patients with acne vulgaris with injections of phenol and have obtained no results.

DR SAMUEL FELDMAN. I have just discharged a patient with moderately severe acne conglobata. I first treated him with roentgen radiation but the results were poor. Injections of alcohol into the abscess cavities helped to clear up the condition which healed with contracted scars and without the breaking down of the skin exhibited by this patient. I believe that one can check the breaking down of these abscesses by using alcohol, this causes the surface to adhere, thus obliterating the cavity.



## PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA Presented by DR. PAUL GROSS

B. D., aged 31, married, presents an eruption which began three weeks ago with a few small lesions on the flexor surface of the wrists and spread gradually to the axillary regions and later to other parts of the body. There is slight itching. The general health of the patient has always been good. There is no history of tuberculosis in the family.

The lesions on the trunk are distributed like an exanthem. On the extremities the flexor surfaces are most involved, but there are some lesions on the extensor surfaces of the forearms and in the deltoid region. The lesions are polymorphous, varying in size from minute yellowish-pink lichenoid papules to more erythematous patches. Scraping of guttate lesions produces a scaly scutulum. In addition there are numerous brownish-red papules with a central vesicle and central necrosis. On the left side of the abdomen there is one lesion, considerably larger than the rest, which shows a central area of necrosis the size of a split pea. The scalp, the face, the mucous membrane, the palms and the soles are free from lesions.

The Wassermann test was negative.

## PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA Presented by DR. MAURICE UMANSKY

L. S., a schoolgirl aged 14, states that her eruption began four months ago with reddish spots on both legs. There are no subjective symptoms.

The patient presents a disseminated maculopapular eruption over the trunk and over the upper and lower extremities. The face, hands and feet are free from lesions. The lesions vary in size from that of a pinhead to that of a pea. They are red-brown, round or oval and slightly raised. Most of the lesions are devoid of scales, a few show a tiny scale. On the front and back of the neck and on the upper part of the chest are numerous lenticular white, depigmented spots resembling leukoderma syphiliticum.

This patient was observed for about eight weeks. During that time many of the earlier lesions faded gradually. Some of the crusted lesions and those showing central pitting healed without scarring.

The Wassermann reaction of the blood was negative.

## DISCUSSION

DR. MAX BERKOVSKY. Apparently this disorder occurs in epidemics. I am prompted to make this statement because at the clinic my co-workers and I at one time observed about three or four cases all at once, and then none were encountered for a year or more.

DR. ARTHUR SAYER. I have observed a few such cases and have studied the development of the eruption. Some lesions appear as papules, and others show papules capped with a vesicle. In most of the cases the disorder is observed when it is in full bloom, and the different types of lesions already present are seen. It is questionable whether some of the lesions begin as ulcers. It is my opinion that the necrotic lesions develop secondarily in papules and that the papule is the primary lesion.

DR. ISIDORE M. LASHINSKY. None of the discussers explained the leukoderma exhibited by Dr. Umansky's patient. In certain cases of varicella one occasionally sees leukodermic spots after the lesion has involuted.

DR. MARION B. SULZBERGER. I have never seen a typical scaly papule of pityriasis lichenoides mutate into a varioliform lesion. I have looked for this mutation, but I do not think that it occurs. In regard to Dr. Lashinsky's question about leukoderma I wish to state that it is common in cases of parapsoriasis and syphilis.

DR LOUIS CHARGIN I have recently observed a case in which there were numerous recurrences in a period of one and one-half years

DR PAUL GROSS I agree with Dr Sulzberger that the varioliform lesions start a priori as exudative lesions and do not result from the typical papules and macules There are four definite types of the varioliform variety of parapsoriasis (1) the acute type without recurrence, (2) the acute type changing to chronic parapsoriasis, (3) the recurrent type, (4) the typical chronic parapsoriasis with occasional appearance of varioliform lesions I do not know any successful method of preventing recurrence Irradiation from the air-cooled quartz mercury vapor arc lamp seems to be a good therapy

DR MAURICE UMANSKY This patient presents an example of the acute variety of pityriasis lichenoides in the stage of involution The residual extensive macular depigmentation, which can be seen, closely resembles and imitates the syphilitic leukoderma There are hardly any distinguishing characteristics which permit differentiation between the leukodermas However, in patients with syphilis the leukoderma rarely reaches the lower portion of the thorax, as it does in this patient

#### A CASE FOR DIAGNOSIS (ULCER OF THE PENIS) Presented by DR THEODORE ROSENTHAL

A S, a Negro, aged 27, married, born in the United States, at the time of admission to the hospital, on April 13, 1935, presented a sore on the penis, which is still present The dark-field examination gave negative results The Wassermann reaction of the blood was 4 plus The patient states that in 1930 he had a chancre on the penis The present sore appeared three months before the patient entered the hospital The total duration of the lesion is therefore nine months Treatment has consisted of eight injections of arsphenamine and twelve injections of bismuth subsalicylate The Wassermann reaction was 3 plus on Oct 14, 1935 The character of the penile sore did not change during the period of treatment

On the ventral surface of the prepuce, visible only on retraction, is a round, whitish glistening lesion about the size of a twenty-five cent piece, with a central depression which admits a probe for about 0.5 cm There is no communication with the urethra The lesion is hard on palpation, it is painless and is not adherent to the underlying structures There are a few small firm glands in both inguinal regions A smear from tissue did not reveal Donovan bodies

A biopsy was performed on Oct 15, 1935 The sections showed large trabeculae of sclerotic scar tissue Individual collagen bundles appeared partially hyalinized This section reminded one of the changes seen in hypertrophic scars and keloids In the interstices of the coarse trabeculae were huge accumulations of mononuclear cells and many plasma cells Small blood vessels were seen to have sclerotic walls and exhibited endothelial changes

#### DISCUSSION

DR DAVID BLOOM This lesion with the hard border looks clinically like an epithelioma I suggest that another specimen for biopsy be taken from the border

DR SAMUEL M PECK The glands are not enlarged, and one would certainly expect that clinical manifestation with a chancre I think that most of the members overlooked the possibility of granuloma inguinale That condition, too, has a marked fibrotic character in some phases With the amount of fibrosis present one must cut the tissue deeply in removing a specimen for biopsy if the organism is to be demonstrated The Giemsa stain should be employed

DR PAUL GROSS The fact that treatment with arsphenamine did not cause the lesion to heal does not speak against syphilis If the disorder is a syphilitic condition it fits more under the heading of chancre redux in other words it could be regarded as a gumma formation at the site of an early syphilitic lesion But I fully agree that it is imperative to perform a more extensive biopsy in

order to exclude the possibility of malignant degeneration. In view of the lack of response to antisyphilitic treatment, administration of potassium iodide or of anionic bismuth is indicated.

DR F E CROSS I am inclined to agree with Dr Bloom that additional biopsies should be made. I do not think that this is the picture of granuloma inguinale. The patient has enlarged inguinal glands, which, as a rule, are not present in patients with granuloma inguinale. The lesion in granuloma inguinale is not quite as hard as the lesion exhibited by this patient, it is not localized, but it has a tendency to spread and has a well defined papular border. I favor the diagnosis of malignant degeneration.

DR W SACHS I think that the lesion is a gumma.

DR DAVID L SATENSTEIN As a rule, I do not make a diagnosis from the examination of a single section. In different sections the process often varies so greatly that one is at times in doubt as to the source of the sections. The picture in the slide I examined is similar to that in a gumma and not to that in a lesion of granuloma inguinale. Clinically the lesion resembles a chancre more than either a lesion of granuloma inguinale or a gumma.

DR ARTHUR SAYER Did the patient receive antisyphilitic treatment for nine months? If he did, I should not be inclined to make a diagnosis of syphilis. I do not believe that a gumma or a lesion of primary syphilis would have failed to respond to persistent therapy.

DR THEODORF ROSENTHAL The patient received eight injections of arsphenamine and twelve injections of bismuth subsalicylate. My first impression was that the condition was an epithelioma. Originally the lesion was larger and annular. Granuloma inguinale was ruled out because no Donovan bodies were found after smears of deep tissue had been made and stained with the Giemsa stain. The histologic examination showed that the lesion is a sclerosing chancre.

#### LEUKODERMA CENTRIFUGUM ACQUISITUM (SUTTON) Presented by DR HENRY SILVER

V F, a woman aged 22, born in Puerto Rico, presents about a dozen depigmented sharply defined oval or round areas with a characteristic central elevated light brown spot. The larger lesions are about 1 or 1½ inches (2.5 or 3.8 cm) in diameter and are situated on the trunk and extremities. There is one lesion on the vulva.

The patient states that the lesions began to appear about two years ago and that they are increasing in size and in number. The personal history is irrelevant.

The Wassermann test of the blood was negative.

The histologic sections showed that the epidermis is practically unchanged except for an absolute lack of pigment throughout the section. In one part of the slide there is an ordinary nevus, but pigment is visible in only one or two of the cells in the nevus itself. The main part of the pathologic process seems to affect the pigment metabolism. The one or two cells containing pigment in the middle of the nests of nevus cells were demonstrated only by the silver stain.

#### DISCUSSION

DR SAMUEL FELDMAN About six months ago I presented a patient at a meeting of this society. That patient had a central reddish-brown spot with a surrounding area of depigmentation. The biopsy showed the central spot to be an intracutaneous pigmented nevus while the surrounding depigmented zone was entirely devoid of pigment. Another patient whom I saw at that time had an eruption of German measles and Sutton's disease on the back. While the skin of the back was uniformly red, the white patch around the nevus remained white. A mustard plaster applied for fifteen minutes over the lesion and including the surrounding normal skin caused the normal skin to become bright red while the nevus remained white as before. My impression is that the whole lesion is a nevus and not vitiligo.

DR W SACHS The entire lesion is a nevus I do not think that such a lesion is rare I think that the central portion contains nevus cells with brown pigment

DR SAMUEL M PECK This is an interesting case In the center of the section are typical nevus cells They too show a lack of pigmentation Even with a silver stain I found that only the nevus cells in the deeper layers of the cutis showed a few granules of melanin I believe that the lesion is a nevus Part of the character of this nevoid formation is a process of depigmentation or rather apigmentation

DR ISIDORE M LASHINSKY I applied mustard plaster full strength for ten minutes on the lesion of Dr Silver's patient, covering the leukodermic spots and the surrounding area The erythematous reaction noticed in the surrounding area could also be seen in the leukodermic spot Whether the duration of the disease has any effect on the capillary response I cannot say, but I do know that in Dr Silver's case the condition persisted for two years while in Dr Feldman's case the duration was much longer

DR MARION B SULZBERGER In Dr Feldman's case there was no response to application of a mustard plaster, apparently because part of the lesion was a naevus anaemicus In pure leukoderma (Sutton) the capillaries are still present, and they should be affected by the irritation resulting from the application of a mustard plaster, as reported by Dr Lashinsky

DR G D ASTRACHAN In a report which appeared about two years ago (*Acta dermat-venereol* **14** 255 [Oct] 1933) Powlow described a case of vitiligo which was accompanied by a typical form of Sutton's disease He expressed the belief that the latter is not a separate entity but some form of vitiligo He also discussed the etiology of Sutton's disease and cited a case in which the disease developed as an after effect of an injury to a peripheral nerve

DR PAUL GROSS One cannot consider the condition as a process confined to the surface of the skin The pigmentary changes are controlled by the vegetative nervous system and by the endocrine glands

DR HENRY SILVER It is difficult to evaluate Dr Feldman's findings In my case the application of a mustard plaster to the depigmented areas elicited redness I have treated three patients with leukoderma (Sutton) with oil of bergamot and ultraviolet radiation with the view of stimulating pigmentation in the vitiliginous areas The treated areas failed to darken, but temporary redness could be easily produced

The central spots are definitely nevi and the histologic observations of Dr Peck corroborated that diagnosis Another feature in this case is the number of pigmented nevi without vitiliginous areas An interesting development would occur if the normal skin surrounding these nevi would in the course of time become depigmented

#### A CASE FOR DIAGNOSIS (LUPUS MILIARIS FACI?) Presented by DR ADOLPH ROSTENBERG

A woman aged 32 single states that the present cutaneous disorder began in May 1935 At that time she presented a butterfly-shaped eruption on the bridge of the nose and on the cheeks The disorder was diagnosed elsewhere as lupus erythematosus The eruption cleared up after the patient received twelve injections of gold sodium thiosulfate

Three weeks ago she had a recurrence There were diffuse redness and slight induration of the nose On the left side of the nose and under the eyelid there were a number of reddish papules the size of a pinhead and one or two small pustules They were of a soft consistency and easily pierced by a toothpick Diagnoses of rosacea-like tuberculid and lupus erythematosus have been considered

## DISCUSSION

DR MARION B SULZBERGER I think that both diagnoses may be considered. The arguments against lupus miliaris faciei are that in that condition the lesions are usually a little larger than the ones exhibited by this patient and often present nodular translucent centers. The distribution in lupus erythematosus is mostly around the nose, and there is telangiectasia. This patient's eruption may be a papular type of lupus erythematosus, but the absence of telangiectasia also speaks against that diagnosis. I believe that histologic examination would be of primary importance in this case. Quantitative tests with tuberculin might also be of diagnostic help. If the disorder is lupus miliaris, the patient may be found to be less sensitive to tuberculin than normal persons.

DR ISIDORE M LASHINSKY My impression is that this patient is suffering from lupus erythematosus. The papular lesions on the nose, however, do not readily fit in with that diagnosis. Perhaps the explanation lies in the fact that this patient received twelve injections of gold sodium thiosulfate and that these lesions represent a reaction to that treatment. I think that the administration of gold sodium thiosulfate should be discontinued and injections of a bismuth preparation should be substituted.

DR ADOLPH ROSTENBERG I have never seen a reaction of this type due to injections of a gold preparation, but if Dr Lashinsky has seen such a result, the atypical lesions may be explained on that basis.

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 LOS ANGELES DERMATOLOGICAL SOCIETY

THOMAS W NISBET, M D, *Secretary*

*Regular Monthly Meeting, Nov 12, 1935*

NELSON PAUL ANDERSON, M D, *Chairman*

## TUBERCULOSIS OF THE SKIN Presented by DR MOSES SCHOLTZ

D C, a woman aged 25, a native of Mexico, says that her disorder started with an abscess of the cervical glands, which appeared when she was 12 years old and has gradually increased in size. The patient is frail, and the skin is transparent, giving an impression of a habitus of tuberculosis. There are multiple small soft, flat deep red nodules bunched together in a patch the size of a plum on the right cheek near the maxilla. There is also some scarring. The patient has been treated with injections of a gold preparation, fulguration, the Gerson-Sauerbruch diet and roentgen radiation.

## DISCUSSION

DR L F X WILHELM I think that the disorder is definitely tuberculosis of the skin. The patient says that she has lived in Mexico City. The disorder apparently started in small lesions, and in thirteen years it has not increased much. Some definite apple jelly nodules are visible.

DR KENDAL FROST I presume this is the type of tuberculosis of the skin which is called lupus vulgaris. It occurs rarely around here. It is an indigenous entity. I think I have seen only one patient in whom it developed here.

DR CHARLES R CASKEY I think I was able to discern apple jelly nodule. It is the nearest approach to such lesions I have seen in Los Angeles.

DR H S CAMPBELL I agree with the diagnosis. The history alone almost establishes it, as the onset was at 12 years of age and followed suppuration of a gland on the side of the neck.

DR H C L LINDSAY I think that in cases of this condition results from medication with a gold preparation are less satisfactory than in cases of lupus erythematosus. The gold preparation can be administered by mouth instead of intravenously. One patient in the Pasadena Hospital who had tuberculosis of the lungs made a wonderful recovery while being treated with a gold preparation.

DR C R HALLORAN A question in regard to treatment with gold sodium thiosulphate in cases of tuberculosis of the lungs arose in the care of a patient to whom I wished to give treatments with that preparation. I began with small and gradually increasing doses. The patient is apparently tolerating the treatment well.

DR MOSES SCHOLTZ This patient was presented not only for diagnosis but for suggestions as to therapy. Lately I am adopting the eclectic method of treatment. I gave the patient injections of small doses of a gold preparation, irradiation, medication with various drugs and diets. She gained 12 pounds (5.4 Kg) and has improved considerably. I sometimes fulgurate those nodules and sometimes give one-fourth unit doses of roentgen radiation. Her physician could not find any evidence of active tuberculosis of the lungs.

#### TUBERCULOUS SARCOID Presented by DR MOSES SCHOLTZ

B G, a woman aged 25, has been in a sanatorium for patients with tuberculosis for the past two years. Her general appearance is fair. On the face, limbs and back there are discrete soft brownish-red plaques from the size of a fingernail to that of a coin. The lesions have been treated with fulguration.

#### DISCUSSION

DR H P JACOBSON I agree fully with the diagnosis as presented. The history of the case, together with the morphology of the lesions, allows little room for difference of opinion regarding the diagnosis. The question of therapy is the important one. About two years ago my attention was directed to a preparation of colloidal copper morrhuate employed extensively in the treatment of tuberculosis, especially in South America. I have since used this preparation in the treatment of cutaneous tuberculosis fairly extensively, and the results have been rather gratifying. I mention this for the benefit of members of the section who have not tried this method of treatment for cutaneous tuberculosis.

DR H C L LINDSAY Some of these lesions were sunken in the center. While the diagnosis of sarcoid may be correct, I have seen granuloma due to bromide look much like these lesions.

DR H S CAMPBELL I agree with the original diagnosis. I do not agree with the statement that lesions of this type can be simulated by eruptions due to bromide.

DR SAMUEL AYRES JR I agree with the diagnosis of sarcoid, but there is not any evidence of tuberculosis in this case. Roentgenograms of the chest show infiltration, but the report states that it is not characteristic of tuberculosis. The patient apparently has chronic sinusitis. There are nasal congestion and postnasal dropping. Whether any case of sarcoid has been reported as due to a nontuberculous infection I do not know, but there seems to me to be a possibility that an infection other than tuberculosis is causing this condition. Chronic sinusitis with postnasal dropping may frequently give rise to thoracic symptoms suggestive of tuberculosis.

DR STANLEY CHAMBERS I agree with the diagnosis of sarcoid. A histologic study of the lesion should be made.

DR MOSES SCHOLTZ For the past three years the patient has been in a sanatorium. Five years ago in Copenhagen, Denmark, I saw a number of patients with sarcoid, but I notice the condition is not rare in this country either. As to the focal infection, it seems to me that in this case the disorder could hardly be regarded as due to focal infection because the lesions show no subacute cellular infiltration. They are stationary and have grown slowly during the last few years.

## MORPHEA Presented by DR SAMUEL AYRES JR

J Y, an American man aged 21, has had fever in August and September as long as he can remember. He underwent tonsillectomy twice. The bowels move daily but are sluggish. Swelling and tenderness of the anterior aspects of the knees were present several years ago, they were thought by an orthopedist to have been caused by flatfoot. The present illness began with a white spot on the right arm, which appeared three months ago. A second lesion appeared about four weeks ago. The patient did not know that any other lesions were present. There are no subjective sensations, and the general appearance is good. There are two lesions on the upper portion of the left arm. The older one is located on the inner aspect, it is about the size of a dollar, is rather ill defined, and consists of a white macule with a suggestion of atrophy and dilated sebaceous orifices which show slight plugging. This white center is surrounded by a poorly defined halo consisting of a pinkish-violaceous narrow zone, and this, in turn, is surrounded by a wider, slightly buff-colored zone. On the outer aspect of the same portion of the arm is a smaller but similar lesion, the line between the white and the halo being rather reticulated. No sebaceous stippling was noted in this lesion. The brownish halo is rather elongated. Throughout this brownish area are seen tiny capillary dilatations. A similar but smaller and less well defined area is present on both upper eyelids and on the front of the neck. None of the lesions are infiltrated. The posterior cervical glands are palpable. Transillumination of the gums and sinuses gave negative results. Microscopic examination of scrapings showed no fungi. The Kahn and Kline tests were negative. The urine was normal except for occasional mucous threads and white blood cells.

## DISCUSSION

DR STANLEY CHAMBERS I agree with the diagnosis of morphea. The atrophy is generally present in certain progressive phases of the disease.

DR MOSES SCHOLTZ I believe that the disorder is morphea in an atrophic stage which shows a large amount of scaling.

DR H S CAMPBELL I agree with the diagnosis. I think that the disorder is of an unusual type. The usual ivory-like induration with the halo around the patches is absent. In this case the areas are distinctly atrophic, the surfaces manifesting a crinkling like that of cigaret-paper. However, the condition would fit in no other category.

DR CHARLES R CASKEY I agree with the diagnosis, but I should like to ask what treatment the patient has received.

DR H P JACOBSON Has a study of the calcium content of the blood been made? In the light of the present tendency of some physicians to connect scleroderma with parathyroid dysfunction I think it would be worth while to check up on the calcium level of the blood in this case.

DR SAMUEL AYRES JR I think this is a case of morphea, although as yet there is no infiltration or thickening. Maybe that will develop later. I have never seen morphea without thickening. The patient has received no treatment recently. In answer to Dr Campbell about the halo, I wish to say that under a good light one can discern a distinct central white or ivory-colored area and a violaceous brownish halo around it. I have not any definite ideas as to what treatment should be employed in this case. I have had one or two patients with morphea who were definitely benefited by ultraviolet radiation from the water-cooled quartz mercury vapor arc lamp with pressure. I should appreciate suggestions as to therapy.

# Directory of Dermatologic Societies \*

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## INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY  
American Secretary Dr Howard Fox, 140 E 54th St, New York

## FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY  
(CANADIAN BRANCH)

H A Dixon, President, Medical Arts Bldg, Toronto, Ont  
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg, Toronto, Ont  
Place Toronto, Ont Time May 1936

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

H W Barber, President, 7, Devonshire Pl, London, W 1  
Louis Forman, Secretary, 7, Devonshire Pl, London, W 1

## NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION  
ON DERMATOLOGY AND SYPHILOLOGY

Harry R Foerster, Chairman, 208 E Wisconsin Ave, Milwaukee  
J Bedford Shelmire, Secretary, 1719 Pacific Ave, Dallas, Texas  
Place Kansas City, Mo Time May 11-15, 1936

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E 54th St, New York  
C Guy Lane, Secretary, 416 Marlborough St, Boston  
Place Kansas City, Mo Time May 11-12, 1936

AMERICAN DERMATOLOGICAL ASSOCIATION

C Guy Lane, President, 416 Marlboro St, Boston  
F D Weidman, Secretary, University of Pennsylvania, Philadelphia  
Place New Ocean House, Swampscott, Mass Time June 4-6, 1936

## SECTIONAL DERMATOLOGIC SOCIETIES

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Samuel Goldblatt, President, 3208 Colerain Ave, Cincinnati  
Raymond G Senour, Secretary-Treasurer, 19 W 7th St, Cincinnati  
Place Cleveland Time Dec 5, 1936

MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

Samuel Goldblatt, President 3208 Colerain Ave, Cincinnati  
Raymond G Senour, Secretary-Treasurer, 19 W 7th St, Cincinnati

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\* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date



NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

Henry J F Wallhauser, President, Medical Tower, Newark  
 Louis J B LeBel, Secretary, 165 Grant Ave, Nutley  
 Place Academy of Medicine of Northern New Jersey, Newark Time Third  
 Tuesday of January, March, May, September and November

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY  
 AND SYPHILOLOGY

Jack W Jones, Chairman, 384 Peachtree St, Atlanta, Ga  
 Winston U Rutledge, Secretary, 332 W Broadway, Louisville, Ky  
 Place Baltimore Time Nov 17-20, 1936

STATE DERMATOLOGIC SOCIETIES

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY  
 AND SYPHILOLOGY SECTION

William H Goeckerman, Chairman, 1680 N Vine St, Hollywood  
 Stanley O Chambers, Secretary, 1210 Roosevelt Bldg, Los Angeles

FLORIDA SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

J L Kirby-Smith, Chairman, 204 Laura St, Jacksonville  
 W M Sams, Secretary, 310 Ingram Bldg, Miami

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M T Van Studdiford, President, 912 Pere Marquette Bldg, New Orleans  
 R. A Oriol, Secretary-Treasurer, Maison Blanche Bldg, New Orleans

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harvey P Towle, President, 453 Marlborough St, Boston  
 Rudolf Jacoby, Secretary, 270 Commonwealth Ave, Boston

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON  
 DERMATOLOGY AND SYPHILOLOGY

Louis Tulipan, Chairman, 224 E 17th St, New York  
 C H Peachey, Secretary, 197 S Goodman St, Rochester

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA  
 SECTION ON DERMATOLOGY

Abraham Strauss, Chairman, Medical Arts Bldg, Philadelphia  
 L G Bembauer, Secretary, 5026 Jenkins Arcade Bldg, Pittsburgh

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY  
 AND SYPHILOLOGY

A E Schiller, Chairman, 10 Peterboro St, Detroit  
 G Warren Hyde, Secretary, 2501 W Grand Blvd, Detroit

MINNESOTA DERMATOLOGICAL SOCIETY

L H Winer, President, 78 S Ninth St, Minneapolis  
 F W Lynch, Secretary, Lowry Medical Arts Bldg, St Paul  
 Time First Wednesday in October, December, February and April

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Marque O Nelson, President, 307 Medical Arts Bldg, Tulsa  
 Harry Green, Secretary, 1116 Medical Arts Bldg, Tulsa

TEXAS DERMATOLOGICAL SOCIETY

J C Michael, President, 1215 Walker Ave, Houston  
 Everett R Seale, Secretary, 1215 Walker Ave, Houston  
 Place Austin

LOCAL DERMATOLOGIC SOCIETIES

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Dudley C Smith, President, University of Virginia Hospital, Charlottesville, Va  
 Francis A Ellis, Secretary, 104 W Madison St, Baltimore

BRONX DERMATOLOGICAL SOCIETY

Eugene F Kelley, Chairman, 93 Radford St, Yonkers, N Y  
 Henry Silver, Secretary, 290 West End Ave, New York

BROOKLYN DERMATOLOGICAL SOCIETY

Samuel Hecht, President, 679 Greene Ave, Brooklyn  
 Mortimer J Cantor, Secretary, 907 St Marks Ave, Brooklyn  
 Time Third Monday of each month except June, July, August and September

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Earl L Eaton, President, 40 North St, Buffalo  
 Richard L Saunders, Secretary, 333 Linwood Ave, Buffalo

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

George M Fisher, President, 264 Genesee St, Utica  
 Rudolph Ruedemann Jr, Secretary-Treasurer, 214 State St, Albany

CHICAGO DERMATOLOGICAL SOCIETY

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 Reuben Nomland, Secretary, 25 E Washington St, Chicago

CINCINNATI DERMATOLOGICAL SOCIETY

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CLEVELAND DERMATOLOGICAL SOCIETY

H G Miskjian, President, 856 Rose Bldg, Cleveland  
 E W Netherton, Secretary, 2020 E 93d St, Cleveland

DETROIT DERMATOLOGICAL SOCIETY

L W Shaffer, President, 1553 Woodward Ave, Detroit  
 William G Saunders, Secretary-Treasurer, 9203 Grand River Ave, Detroit

LOS ANGELES DERMATOLOGICAL SOCIETY

N P Anderson, Chairman, 2007 Wilshire Blvd, Los Angeles  
 Thomas W Nisbet, Secretary, 65 N Madison Ave, Pasadena, Calif  
 Time Second Tuesday of each month, October to May, inclusive

MANHATTAN DERMATOLOGIC SOCIETY

Paul E Bechet, Chairman, 55 Park Ave, New York  
 Mihran B Parounagian, Secretary, 126 E 39th St, New York

MONTREAL DERMATOLOGICAL SOCIETY

Alberic Marin, President, 1414 Drummond St, Montreal, Canada  
Paul Poirier, Secretary, 2073 St Denis St, Montreal, Canada

NEW ENGLAND DERMATOLOGICAL SOCIETY

William P Boardman, President, 388 Marlborough St, Boston  
J Harper Blaisdell, Secretary, 45 Bay State Road, Boston

NEW YORK ACADEMY OF MEDICINE, SECTION OF  
DERMATOLOGY AND SYPHILIS

Max Scheer, Chairman, 509 Madison Ave, New York  
Frank C Combes, Secretary, 80 W 40th St, New York

NEW YORK DERMATOLOGICAL SOCIETY

R H Rulison, Chairman, 114 E 62nd St, New York  
Eugene F Traub, Secretary, 140 E 54th St, New York

OMAHA DERMATOLOGICAL SOCIETY

Charles McMartin, Chairman, 611 City National Bank Bldg, Omaha  
Donald J Wilson, Secretary, 1216 Medical Arts Bldg, Omaha

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Herbert J Smith, Chairman, 3305 N 17th St, Philadelphia  
Vaughn C Garner, Secretary, Greene and Coulter Sts, Philadelphia

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## LXXIII—CUTANEOUS TORULOSIS

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AND

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The incidence of cutaneous torulosis, both in the United States and in Europe, has not as yet reached a point alarming to the physician and the layman. This disease is rare—at least its occurrence has rarely been reported in the literature—and needs closer attention than has heretofore been paid to it with regard to differential diagnosis. The infection usually manifests itself on the skin, as pointed out by Wile,<sup>1</sup> in the form of acneform pustules, granuloma-like ulcers, deep-seated abscesses and nodules, the last-mentioned lesions varying in size and showing no tendency to ulceration.

Clinically the condition is worthy of a great deal of investigation chiefly because it may simulate closely the lesions of blastomycosis and coccidioidal granuloma, particularly the European blastomycosis of Busse and Buschke. The correct differential diagnosis of these conflicting infections depends usually on the determination of the invading organism by the methods described by Weidman.<sup>2</sup> Such laboratory procedure, however, must be carried out by a person well trained in mycology. A number of yeastlike fungi may be found in cutaneous

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The case reported is from the Department of Neurological Surgery, School of Medicine, Washington University, Service of Dr. Ernest Sachs.

Studies, observations and reports on cutaneous aspects from the Barnard Free Skin and Cancer Hospital, and the School of Medicine, Washington University, Department of Dermatology and Syphilology, Service of Dr. M. F. Engman and Dr. W. H. Mook.

\* This paper was intended for publication by Dr. William H. Mook before his death, which occurred on Nov. 3, 1934. Owing to the complications of routine and investigative work that was in progress the material was set aside for such a time as would permit its complete preparation. After Dr. Mook's untimely death the data seemed of sufficient interest to warrant the completion and publication of the report.

<sup>1</sup> Wile, U. J. Cutaneous Torulosis, *Arch. Dermat. & Syph.* **31**: 58 (Jan) 1935.

<sup>2</sup> Weidman, F. D. Cutaneous Torulosis, *South. M. J.* **26**: 851, 1933.

lesions which under satisfactory conditions may present a picture analogous to that demonstrated for the organism causing torulosis. This is particularly evident in infections produced by some of the imperfect yeasts, which are often confused with *Cryptococcus* and *Zygomycetes* (*Endomyces*). The response of tissue to these invading microbes varies considerably, but the fungus itself may, and usually does, develop a mucoid capsule around itself, which is demonstrated in india ink preparations as a clear, gelatinous sheath or envelop. The thickness of this so-called capsule varies, but it rarely, if ever, reaches the proportions found in *Cryptococcus histolyticus*. This feature serves best to differentiate true torulosis from many of the diseases due to contaminating yeastlike organisms.

It is unfortunate that the term torulosis has been completely adopted by the medical profession to indicate a particular infection caused by a yeastlike organism which apparently is misnamed. The generic term *Torula* as applied to the causative agent of this disease is incorrect and should be replaced by the term *Cryptococcus*, as will be pointed out in this paper. For the sake of nomenclatorial correctness and with the hope that the term *C. histolyticus* will come into universal usage, this term is used throughout this paper.

Torulosis as a clinical entity was first believed to be confined to the internal organs, particularly the brain and the spinal cord. As such it has received a great deal of attention in extensive monographs, the first of which was published by Stoddard and Cutler,<sup>3</sup> which included a clinical review and experimental and cultural data with regard to the fungus. The authors stressed the absence of cutaneous involvement. The most recent review in monographic form is that by Freeman.<sup>4</sup> This work is a fine treatise on the histopathologic features of the disease.

The known cases of supposed torulosis of the skin have been reviewed by Weidman<sup>2</sup> and Wile<sup>1</sup> but brief mention of them will be made here. The first case of cutaneous torulosis was reported by Rappaport and Kaplan<sup>5</sup> as having occurred in a patient who died of generalized torulosis. The disease had involved the cerebrospinal system, lungs and other internal organs. The skin showed symptoms later in the form of an acneiform pustule on the forehead. Cultures of *C. histolyticus* were grown from these lesions. The cutaneous manifestations were found histologically to be located in the corium and to consist of infiltrations of fibroblasts, round cells, many organisms and a generalized

3 Stoddard, J. L., and Cutler, E. C. *Torula Infection in Man*, Monograph 6, Rockefeller Institute for Medical Research, 1916, p. 1.

4 Freeman, W. *Torula Infection of the Central Nervous System*. *J. Psychol. u. Neurol.* **43**: 236, 1931.

5 Rappaport, B. Z., and Kaplan, B. *Generalized Torula Mycosis*, *Arch. Path.* **1**: 720 (May) 1926.

chronic reaction. This picture simulates closely that seen in the case reported in this article.

A doubtful case of torulosis of the skin is that reported by Veise.<sup>6</sup> In this case, there appeared on the body of the patient acneiform lesions which later degenerated into ulcers. The patient died of meningitis, and a diagnosis of systemic blastomycosis was made. Autopsy showed a possible generalized torulosis. This case, however, cannot be definitely considered as one of cutaneous torulosis, as concrete evidence was lacking.

In the same year that Rappaport and Kaplan reported their case, McGehee and Michelson<sup>7</sup> reported an infection occurring in a Negress. The patient had a localized abscess, with pain and swelling, in the left groin. Cultures of *C. histolyticus* were grown from this lesion. There were no systemic or generalized symptoms, and the patient recovered. It is possible that the organism which answered the description of *Cryptococcus* may have been a weak strain. On the other hand, one cannot rule out the possibility that a saprophytic strain of *Cryptococcus*, so common on the skin, may enter into a small lesion and there live on debris and multiply rapidly, causing pain and swelling.

The most outstanding case of supposed cutaneous torulosis is that reported by Urbach and Zach.<sup>8</sup> The disease had its origin in the mouth. The lesions spread to the upper jaw and, approximately one year later, to the abdomen, lungs, thigh and neck. The left jaw showed firm, indolent lymph nodes with purplish nodules the size of lentils on the cheek. Large numbers of budding cells were cultured. Histologic examination showed epithelioid and plasma cells and many giant cells, within which were the fungi. The patient died approximately two years after the onset of the disease, of cerebrospinal involvement. Yeastlike fungi were cultured from the spinal fluid, brain, sputum, urine, palatal fistula and thigh.

The organism cultured from the thigh and that cultured from the spinal fluid were identical, whereas that obtained from the brain showed a difference in color. The cultures sent by Zach showed that when cultured on agar these fungi developed into elongated cells as described in a previous paper,<sup>9</sup> and hence that they were not typical of *C. histolyticus*. They resembled more the organism causing the

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6 Veise, M. Ueber einen Fall von allgemeiner Blastomykose beim Menschen. *Verhandl. d. deutsch. path. Gesellsch.* **17**: 275, 1914.

7 McGehee, J. L. and Michelson, I. D. Torula Infection in Man. *Surg., Gynec. & Obst.* **42**: 803, 1926.

8 Urbach, E., and Zach, F. Generalized Torulosis. *Arch. i. Dermat. u. Syph.* **162**: 401, 1930.

9 Moore, M. A Study of *Endomyces Capsulatus*. *Rewbridge Dodge and Myers. A Causative Agent of Fatal Cerebrospinal Meningitis.* *Ann. Missouri Bot. Gardens* **20**: 471, 1933.

European type of blastomycosis of Bussey and Buschke. The organism from the sputum acquired a violaceous color when cultured on agar, which may account for the color of the lesions in the mouth and jaws. This organism differed from the others. A red yeast, isolated from the lungs and from the urine, had definitely no relationship to the others, except possibly, to a certain degree, in morphology. The fungus from the palatal fistula differed in that it was much smaller than the others.

It is possible that there were several complicating infections in the one patient, but it could not be said that the disease was a typical torulosis both of the brain and of the skin. Certainly, the microbes did not indicate the relationship. This, however, does not detract from the clinical value of this interesting case.

In 1932, at a meeting of the Atlantic Dermatological Conference (November 11), Weidman<sup>10</sup> reported a case of experimental torulosis in a monkey. In the discussion one of us (Dr. Mook) referred to the case described in this paper.

Three years later Wile<sup>1</sup> reported a case of cutaneous torulosis in a boy. In addition to unusual patches of lesions on the backs of the thighs and behind the knees, the patient had psoriasis and multiple verrucae. The peculiar lesions were hard and infiltrated. A biopsy of material from a nodule showed many giant cells and a large number of yeastlike, double-contoured budding cells. There apparently was no inflammatory reaction. It is unfortunate that a mycologic study of the parasite could not be made in this case. The illustrations accompanying Dr. Wile's paper point to an organism which may be closely related to *C. histolyticus*, but the response of tissue, the huge number of giant cells and the particular morphologic characteristics of the cell within the tissue indicate that a different organism may have been involved. In any case, the possibility of cutaneous torulosis is not as rare as the literature seems to indicate.

The case reported here is of interest for two reasons. 1. The lesion, which occurred on the toe, was conical and crusted and could not be differentiated clinically from an ordinary infectious granuloma. 2. Histologic examination showed a number of typical organisms of torulosis of the brain, with huge gelatinous or mucoid capsules, occurring in the skin both in the corium and in the epidermis.

#### REPORT OF CASE

*History and Course*—The patient, a well developed man, aged 43, entered the Barnes Hospital on Jan. 27, 1932. He complained of pain in both eyes, attacks of dizziness, lack of hearing, which had been present for two months and was

particularly marked in the left ear, pain in the back of the neck for one and a half months, and poor sleep for one month

The patient came to the United States at the age of 22 and worked in an iron foundry for fifteen years. During that time his hearing began to fail, and he noticed a diminution in sound effects. There was no history of any injury or buzzing in the ear. The deafness was accentuated in 1931, when the patient's older son died of tuberculosis. For five years before admission to the hospital the patient had worked in a shoe factory, and during that time he complained of neuralgia-like pains. Relatives stated that since the death of his son the patient had become reticent and was not his former self. He also complained of diminution in vision and of some blurring of objects. This gradually increased, and for a month and a half he had trouble at his work. The last month before admission to the hospital he became restless and could not sleep at night because of the pain in both eyes. The last two weeks he had attacks of dizziness while at work. He never fainted or vomited, but he was nauseated and had to lie down.

On admission there were severe headaches, chiefly in the occipital and frontal regions, which were worse at night. There was evidence of a progressive loss of vision, with occasional diplopia. The patient complained of attacks of dizziness and pain in the eyeballs and in the back of the neck; he stated that the objects in the room appeared to move away from him. He pointed to his forehead as the region of pain. His deafness gradually increased until he could barely hear shouting. He complained of ringing in the ears and had increasing vertigo. His appetite became increasingly worse, but the lack of appetite was not associated with pain, vomiting, constipation or the presence of blood in the stools. It was, however, associated with attacks of dizziness. Friends noticed that the patient's speech was slower than normal. There were no lapses of memory and no defects of speech.

In summary, the pathologic findings were bilateral amblyopia associated with vertigo, diplopia, choking of both optic disks, obtundity of disk sensations, vertical nystagmus and upper gaze, bilateral tinnitus and deafness, the impairment being greater on the left side, some slowness of speech, and a questionable Babinski sign on the right side.

Roentgen examination of the skull was made on January 28. Lateral stereoscopic films of the skull (right side of the skull to the film) and antero-posterior films (Towne position) were made. The skull was symmetrical, the sella was within normal limits. There was increased density in the parietal region, which was somewhat greater than normal, and a slight convulsional atrophy was noted throughout the calvaria. There were symmetrically placed large areas of calcification within the region of the choroid plexus in both lateral ventricles. There was a small amount of calcification in the midline, which appeared to be in the region of the pineal body. There was a slight suggestion of erosion of the dorsum sella. The film taken in the Towne position added nothing to the foregoing observations though it corroborated the localization of an intracranial calcification noted in lateral stereoscopic films. There was no evidence of erosion or change in the petrous portion of the temporal bone on either side.

The roentgen diagnosis was increased intracranial pressure.

The patient's stool was found to contain *Hymenolepis nana* (rat tapeworm).

*Operation*—On Feb. 3, 1932 surgical intervention was resorted to. Tri-bromethanol in amylene hydrate supplemented by local anesthesia was used and a flap was outlined beginning in the medial line in the forehead and going back



to a point above the ear on the right side and then down into the temporal fossa. The flap was reflected, the dura was not very tight. In the anterior region it felt soft, as though there might be a cyst beneath it. An incision was made, and the cortex was examined, but no cyst was found. The olfactory nerve was exposed, but no tumor was found. The frontal lobe was reexamined, higher up, and a tumor about the size of a pea was found in the cortex. An area about the size of a 25 cent coin was circumscribed and cut out when it was thought that sufficient depth had been allowed for the excision. A tumor, the size of a small cherry, was removed in toto. It resembled a glioma.

*Pathologic Examination of Excised Tissue*—The tumor was examined in the laboratory of the Barnes Hospital on February 3.

*Macroscopic Examination* The material consisted of a fairly well demarcated bluish-gray tumor, about 1.5 cm in diameter and harder than the surrounding brain tissue.

*Microscopic Examination* Sections stained with hematoxylin and eosin showed a lesion with a definite outline of demarcation from the surrounding brain tissue.



Fig. 1—Lesion of cutaneous torulosis on the second toe.

The lesion was composed of a loose tissue having in it many round bodies, which varied in size. Some were slightly larger than the lymphocytes, and others had a diameter equal to that of a moderate-sized blood vessel. Around each body was a clear area devoid of tissue. Each round body (organism) had a large granular central area, surrounded by an area which was refractile with hematoxylin and eosin but stained deep orange with phosphotungstic acid. In the surrounding tissue were many round cells, plasma cells and fibrinosis. No polymorphonuclear leukocytes were present. There was a slight increase in glial nuclei in the adjacent brain substance.

A diagnosis of torulosis of the brain was made.

*Subsequent Pathologic Observations*—Examination of the spinal fluid on Feb. 26, 1932, showed C. histolyticus.

One of us (Dr. Mook) noticed that on the plantar surface of the second toe of the right foot there was a definitely elevated tumor-like mass 0.6 cm in diameter, conical, crusted and a little scaly (fig. 1). The lesion was infiltrated, it was considered to be due to a local infection, probably staphylococci. Dr. Mook diagnosed it as an infectious granuloma and advised actual cautery.

The tumor was excised at the Barnes Hospital on Feb. 29, 1932. Grossly it was seen to consist of small pieces of reddish-gray friable tissue. Microscopic

sections showed small pieces of squamous epithelium and corium. In the corium there was an infiltration of lymphocytes, plasma cells and leukocytes. Throughout the tissue were many round bodies, varying in size. Around each there was a clear zone with a large granular area in the center. Some of these bodies were found in the epithelium, but the greatest number occurred in the epithelial connective tissue (figs 2, 3 and 4).

A diagnosis of torulosis of the skin was made.

*Discharge and Subsequent History*—The patient was discharged under protest on Feb. 29, 1932.



Fig. 2—Low power magnification of a section of skin stained with hematoxylin and eosin, showing many organisms in the corium.

The patient was readmitted on March 4, 1932. During the interim while he was at home he had a great deal of headache in the frontal region, the pain was most pronounced in the suborbital region and was practically constant. These headaches had become so severe that the patient had difficulty in sleeping at night. There had been no noticeable visual disturbances, convulsions, seizures or progressive weakness during this period. The patient's appetite had been poor, and marked constipation had been present. He returned to the hospital because of the intractability of the aforementioned symptoms.

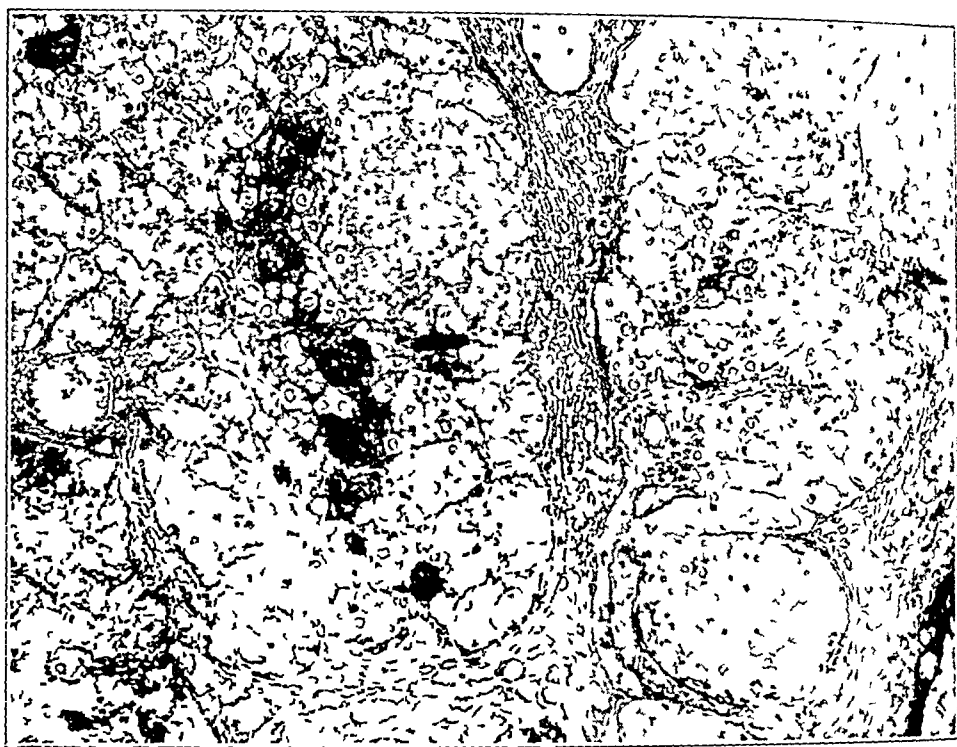


Fig 3—Low power magnification of a section stained with hematoxylin and eosin, showing a fibrosed condition and many encapsulated fungi in the epidermis and corium

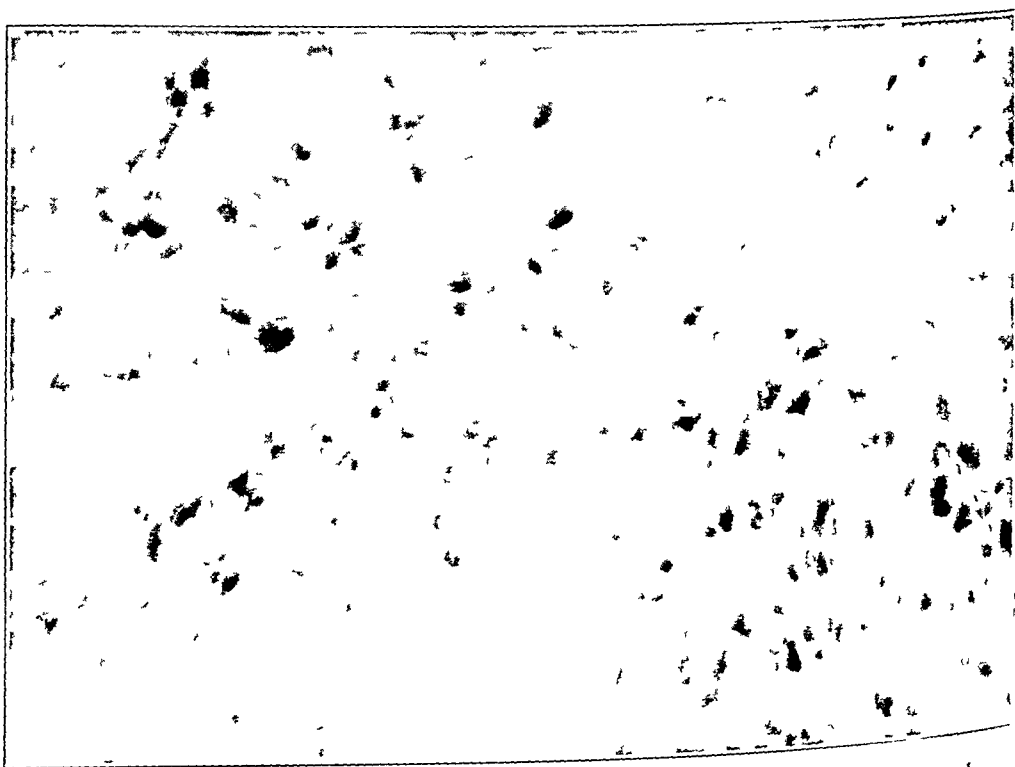


Fig 4—High power magnification of a section stained with hematoxylin and eosin, showing *C. histolyticus*

The positive findings were subtemporal decompression on the right side, with absence of marked bulging, bilateral choked disk, facial weakness on the left side, bilateral deafness, an Oppenheim sign on the left side, and a Romberg sign.

On April 10 it was noted that the patient was rapidly failing. He had several pressure spots on the back. He was becoming more and more stuporous. Choking of the disks had increased tremendously.

By May 1 decubitus ulceration was worse and was present over each trochanter. The patient talked at times, he took food fairly well. The fundi showed marked choking, with great profusion of hemorrhages and exudate.

The patient died on June 13.

*Final Note*—Dr Sachs summarized the case as follows. The disease ran a course similar to that reported in the literature on torulosis. The unusual features in the case were (1) the presence of cutaneous lesions due to *C. histolyticus*, (2) the presence of a rat tapeworm which caused some confusion in the diagnosis in early stages of the disease.

*Autopsy*—The following conditions were found at autopsy: (1) generalized torulosis involving the skin, brain, lungs and kidneys; (2) otitis media on the right side with involvement of the mastoid cells; (3) defect in the frontal lobe from an old craniotomy; (4) subtemporal decompression; (5) herniation of the right orbital lobe; (6) scaling of the myocardium; (7) clubbing of the fingers; (8) moderate arteriosclerosis; and (9) chronic pneumonia and bronchiectasis.

#### COMMENT

The organism isolated from the spinal fluid, brain and lesion on the toe were identical and morphologically and physiologically conformed to the characteristics of *C. histolyticus*. Several months after isolation and culture the fungus showed no mycelium or endospore formation. The carbohydrate reactions were still characteristic. Unfortunately, the cultures dried and could not be subcultured. We feel certain, however, that the microbe was *C. histolyticus*.

There is much discussion as to the correctness of the terms *Torula* and *Cryptococcus* in reference to the causative agent of torulosis. Owing to usage, the term *Torula* has rapidly supplanted the correct term *Cryptococcus*. This change would not be at all incongruous were it not that the genus *Torula* has a distinct and entirely different appearance from that shown by the organism of the disease torulosis. The original description of the genus *Torula* given by Persoon<sup>11</sup> reads: "effusa, acaulis, filis articulatis indeterminate effusis mucidis." Lindau,<sup>12</sup> in Rabenhorst's *Kryptogamen Flora* gave the following more complete description of this genus:

sterile hyphae lacking or mould-like spread out, branched, septate, hyaline or darkly colored. Conidiophores either completely lacking or developed as short branches. Conidia developed either through disarticulation or the complete

11 Persoon, D. C. H. *Synopsis methodica fungorum* Göttingen 1801 p. 693.

12 Lindau, G. in Rabenhorst *Kryptogamen Flora* Pilze VIII 1904-1907 *Fungi imperfecti* Leipzig Eduard Kummer 1907 p. 567.

filaments as gemmae or by sprouting on the mycelium and then multiplying as budding colonies, or by growing out in long chains at the base of the tips of mycelial branches. The conidia are then comprised of attached chains, which finally break apart in single cells or short, jointed segments, mostly black, brown, olive-green or gray, spherical, elongated, ovoid or spindle-shaped, smooth or rough to warty.

The following material taken from Dodge<sup>13</sup> discusses exactly the existing knowledge with reference to *Cryptococcus*.

The aforementioned description differs completely from that given originally for the genus *Cryptococcus* by Kützing<sup>14</sup> in his "*Algarum aquae dulcis germanicarum Decas III*" and then in "*Linnaea*"<sup>15</sup> as follows: "*Globuli mucosi hyalini non colorati microscopici in stratum indeterminatum mucosum facile secedens sine ordine aggregati*" He gave as his type species *Cryptococcus mollis* Kützing occurring "on moist and dirty windows."

The description is accompanied by an illustration of a specimen dried to a small square of glass. The fungus consists of hyaline, thin-walled spores. There is also present, obviously as a contaminant, a small amount of a slender mycelium with small, slightly colored, thick-walled spores, probably a saprophytic species of *Absidia*, which agrees with the specimen of Kützing's *Leptomitum plumula* issued in *Decas I*, no 9. The exact habitat is not given, but, judging from the fact that Kützing referred to this species as found in conjunction with his *L. plumula*, it seems probable that the organism was found on dirty windows, always in the shadow from the building opposite, in the courtyard of an inn in Herbsleben, a hamlet of Gotha, Germany. Kützing, still laboring under the misconception that these groups are polymorphic, thought that his species of *Cryptococcus* was close to the primordial slime of the philosophers and that various higher forms might develop from it, for he mentioned that on a well lighted window *Oscillatoria* developed and gradually replaced the *Cryptococcus* colony. Since, in general, the species of *Oscillatoria* require a considerable amount of organic nitrogen for their active development, it seems quite likely that the habitat where he found his species of *Cryptococcus*, namely, in water of condensation on windows of farmers' living rooms and inn yards, might easily have been contaminated by dirt from the stables. This supposition is also strengthened by the presence in the type collections of tiny, brown particles of dirt, which under the microscope appear to be bits of dung. Hence, it is quite possible that from the first the generic name *Cryptococcus* has been associated with an imperfect yeast.

13 Dodge C W. Medical Mycology, St. Louis C V Mosby Company, 1935.

14 Kützing. *Algarum aquae dulcis germanicarum Decas III*, no 28 1831, cited by Dodge<sup>13</sup>.

15 Kützing. *Linnaea*, 1833, vol 8, p 365.

from the intestinal tract, if not with some more active parasite of the domestic animals

Kutzing mentioned in his publication a number of other species of *Cryptococcus*, but in 1849 he again discussed the genus in his "Species Algarum"<sup>16</sup> and still expressed the opinion that the typical members are spherical, shiny and found in moist habitats

In the following years the generic name fell into disuse, owing, in part, to lack of interest on the part of mycologists and to the misconceptions of Persoon's *Torula* and *Mycodeima* by Desmazières, Tuipin and Hansen

In 1901 Vuillemin revived the name *Cryptococcus* for the asporogenous, nonfermenting yeasts from animal substrata, and since then the name has been used by the medical profession. The genus may be described as follows. The cells are spherical, ovoid or ellipsoid, occurring singly or held in more or less irregular groups by the secretion of thick, gelified capsules, especially in old age. The organism does not form ascospores, mycelium or pseudomycelium. On liquid mediums, the pellicle is thick, formed by the coalescence of slimy, floating islets when present, and the sediment is usually slimy. There is no fermentation with carbohydrates, and acidity is rare. Liquefaction of gelatin is slow when present.

Stoddard and Cutler,<sup>3</sup> under the guidance of Wolbach, first brought the pathologic picture to general attention, but they did not attempt to isolate the organism from material obtained from their patients and based their experimental work on species of this genus isolated more than a decade previously from lesions in the lung of a horse. They assumed that an organism which produced a pathologic condition in experimental animals similar to that found in man must necessarily be the same species as that with which they had produced the disease in man. The work of Freeman<sup>4</sup> indicates that there are probably three, or perhaps more, organisms which produce the same general pathologic condition, differing in minor respects. However, until there is more careful correlation of pathology and cultural characters, the nomenclature of this group must be unstable. Up to the present, only about half the pathologists who reported cases have described cultures of the organism isolated, and in not a single case has it been adequately described, while the only adequate description is not accompanied by a case history or a description of the pathologic changes.

It can be easily seen from these original descriptions that *Cryptococcus* is the correct generic name and should in all cases be used in preference to *Torula*.

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<sup>16</sup> Kutzing. *Species Algarum*. Leipzig. p. 145. 1849.

## SUMMARY

A case of fatal torulosis of the brain with a distinct and definite involvement of the skin is reported

The known, published cases of cutaneous torulosis are reviewed with comments

The cutaneous lesion is described as resembling an infectious granuloma

The original descriptions of *Torula* and *Cryptococcus* are discussed, and it may be concluded that *C. histolyticus* is the correct term to be used for the causative agent of torulosis. This does not imply that *C. histolyticus* is the only species, however, for there may be other species of *Cryptococcus* that cause this same condition

This report represents the third definitely known case of cutaneous torulosis, bringing the total of such cases possibly to five

# PUSTULAR PSORIASIS

ITS RELATION TO ACRODERMATITIS CONTINUA VEL PERSTANS

FRANCIS A ELLIS, M D

BALTIMORE

In 1888 Radcliffe Crocker<sup>1</sup> first described acrodermatitis repens. Two years later Hallopeau<sup>2</sup> reported a case of chronic suppuration of the fingers of a patient who had Raynaud's disease. The pustules were not confined to the digits affected by the vasomotor disturbances but were present on other fingers and on the mucous membrane of the mouth. The lesions were superficial, they involuted rapidly and dried within twenty-four hours. Two years later Hallopeau reported another case, in a patient who had had a benign form of psoriasis since childhood. The pustular eruption appeared on the left thumb after an injury caused by a blow of a hammer. Within two years the eruption spread and involved the other digits and the palm. Staphylococci were present in the lesions.

More recently the literature has been reviewed and added to by Ingram,<sup>3</sup> Audry,<sup>4</sup> Dore,<sup>5</sup> Barber and Eyre,<sup>6</sup> Barber,<sup>7</sup> Bloom<sup>8</sup> and others. Bloom reported four cases of so-called pustular psoriasis of the palms and soles in patients who did not have psoriasis on any other part of the body.

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Presented before the Baltimore-Washington Dermatological Society, Feb 21, 1935

1 Crocker, H Radcliffe Diseases of the Skin, London, H K Lewis & Co, Ltd, 1888, p 128

2 Hallopeau, M H Sur une asphyxie locale des extremités avec polydactylite suppurative chronique et poussées éphémères de dermatite pustuleuse disséminée et symétrique, *Bull Soc franç de dermat et syph* **1** 39 (June) 1890

3 Ingram, John T Acrodermatitis Perstans and Its Relation to Psoriasis, *Brit J Dermat* **42** 489 (Nov) 1930

4 Audry, C Les phlyctenoses récidivantes des extrémités (acrodermatites continues de Hallopeau), *Ann de dermat et syph* **2** 913, 1901

5 Dore, S E Note on Cases of a Chronic Mild Localized Type of Acrodermatitis Perstans, *Brit J Dermat* **40** 12 1928

6 Barber, H W, and Eyre, J W H Acrodermatitis Continua (Hallopeau) Vel Dermatitis Repens (Crocker), *Brit J Dermat* **39** 485, 1927

7 Barber, H W Acrodermatitis Continua Vel Perstans (Dermatitis Repens) and Psoriasis Pustulosa, *Brit J Dermat* **42** 500 1930

8 Bloom, David Pustular Psoriasis of the Palms and Soles Report of Four Cases, *Arch Dermat & Syph* **32** 90 (July) 1935



A controversy arose as to the exact status of this disease and its relation, if any, to psoriasis, or more specifically to pustular psoriasis. Various investigators have in the presentation of cases attributed the condition to staphylococcal infection, psoriasis and neurogenic disturbance, and some have considered it a disease sui generis. Barber with his extensive experience, has attempted in his contribution to the literature to give a comprehensive picture of pustular psoriasis and acrodermatitis continua (Hallopeau) vel repens (Crocker), but occasionally a patient is seen whose condition defies definite differentiation and seems to bridge the gap between these two diseases. Such a case is presented here.



The superficial pustules, the granulating, distorted ends of the fingers and the fixed, useless hand are shown in detail. Note that the phlyctenules extend into the psoriasis on the flexor surface of the forearm. A biopsy specimen was taken from the area marked A.

#### REPORT OF A CASE

C. B., a white man aged 40, was first seen at the St. Agnes Hospital in the service of Drs. Bloodgood and Cohn, in December 1933. Ten years before while the patient was living on a farm in Canada, his left hand was severely frost bitten. Soon afterward pustules developed about the nails of the left hand, and these had persisted up to the time of the patient's admission to the hospital. At times the condition tended to improve during the summer but the tendency had been for it to become continually worse. Large plaques of psoriasis developed on the scalp, chest, abdomen and upper extremities eighteen months before the patient's admission to the hospital. The left arm was extensively involved, and the phlyctenule on the hand and wrist extended up into the psoriatic tissue. The entire left hand and wrist were covered with many superficial pustules on a pale pink inelastic skin. Several nails of the left hand were missing leaving rounded granulating

stumps at the ends of the fingers, while other nails were small, distorted, rough, brittle and thickened. The hand and fingers were fixed and useless. On physical examination no other abnormality was disclosed.

The Wassermann reaction of the blood and the reaction to 0.1 cc of a 1:50 solution of trichophytin given intradermally were negative. The blood was essentially normal. Culture of material from unruptured phlyctenules repeatedly yielded a pure growth of staphylococci. Mycelia or yeast were not seen on direct examination or in cultures. Roentgenograms of the left hand showed atrophy of the bones due to disuse, but no evidence of periostitis was discernible.

The numerous biopsies of specimens from the tips of the fingers, which were made in order to rule out the possibility of the presence of a malignant process,

*Salient Features of Acrodermatitis, Pustular Psoriasis and Condition in the Case Reported\**

Acrodermatitis Continua	Pustular Psoriasis	Condition in Case Reported
1 Unilateral infective post traumatic lesions situated at ends of digits	1 Usually bilateral lesions seldom any history of injury	1 Unilateral lesions, left hand and fingers affected after severe frost bite
2 Lack of symmetry even if bilateral	2 Striking symmetry	2 Unilateral lesions
3 Involvement of nails, early and prominent, with loss of nails	3 No involvement of nails or psoriasis of nails	3 Involvement of nails from start, with loss of some nails
4 Frequent involvement of mucous membranes	4 No involvement of mucous membranes	4 No involvement of mucous membranes
5 More or less circular elementary lesions, rapidly enlarging subcorneal abscesses, which strip up the horny layer as they extend peripherally	5 Elementary lesion red dened areas, in which form intra epidermic pustules, the size of a pinhead, some of which may become confluent, the majority drying up in situ to form minute brownish "scabs"	5 Elementary lesions often annular, rapidly formed subcorneal abscesses which raised the horny layer as they extended
6 Staphylococci abundant in cultures	6 Sterile cultures	6 Abundant pure growth of staphylococci on repeated culture (mediums inimical to ordinary strains were not used)

\* The first two columns are adapted from the table given by Barber.

showed only chronic inflammatory tissue with many fibroblasts. A specimen for biopsy was taken from the flexor surface of the left forearm, where several pustules were located in a plaque of psoriasis. Under low magnification dense collections of leukocytes were seen just under the stratum corneum, with a slight amount of fluid in some of the small pustules. Only rarely did the infiltrate penetrate into the rete. The even regular acanthosis was striking, the pegs usually approached within four or five rows of cells of the horny layer. These pegs contained a moderate number of leukocytes but about the tips of the inter-papillary pegs the infiltrate was denser. An unusual feature was the number of leukocytes and fibroblasts in the middle and deeper parts of the corium. Many dilated hyperplastic capillaries also were present in these parts of the cutis. Under high magnification little intracellular and intercellular edema was seen in the epidermis even in the areas adjacent to the subcorneal pustules. The leuko-

cytes seemed to migrate through fissures in the rete (tunneling of Civatte<sup>9</sup>). The infiltrate in the cutis was composed predominantly of polymorphonuclear leukocytes, with many early fibroblasts about the dilated capillaries. The collagen was fragmented or split into long narrow ribbons, and the elastic tissue was completely destroyed.

The salient histologic features were the large Muro-Sabouraud abscesses, the lack of edema in the rete, marked regular acanthosis and the extensive early fibrosis of the cutis.

#### COMMENT

Barber<sup>7</sup> presented a table showing the points in the differential diagnosis between acrodermatitis continua and pustular psoriasis, which is given in abridged form here (table), with the addition of a third column showing the salient features in the case reported. The condition in this case differed from acrodermatitis continua in only one essential feature, that lesions were not present on the mucous membranes. It should be noted that involvement of the mucous membranes is often lacking in cases of acrodermatitis continua. Bloom expressed the belief that pustular psoriasis and acrodermatitis continua are identical.

#### SUMMARY AND CONCLUSION

Although Barber seemingly gave a convincing, clearcut differential diagnosis between acrodermatitis repens vel continua and pustular psoriasis, occasionally a condition is seen which defies differentiation. A case of psoriasis is reported in which the condition was complicated by a unilateral superficial pustular eruption after severe frost-bite of the hand. The eruption had the features which Barber considered characteristic of acrodermatitis continua. From the literature and the case reported one must conclude either that acrodermatitis continua is a form of pustular psoriasis or that the patient had had acrodermatitis continua for ten years and psoriasis developed later.

104 West Madison Street

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9 Civatte, A. Psoriasis and Seborrhoeic Eczema. *Pathological Anatomy and Diagnostic Histology of the Two Dermatoses*, Brit J Dermat **36** 461, 1924.

# FAMILIAL XANTHOMA

## REPORT ON THREE OF FIVE SIBLINGS WITH XANTHOMA TUBEROSUM MULTIPLEX

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AND

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Seventeen reports on familial xanthoma, comprising a total of fifty-two cases, have been published <sup>1</sup>

The condition is transmitted as a recessive characteristic and may be inherited through either parent. Six times it has been reported as occurring in two siblings and no other relatives,<sup>2</sup> and twice it has been noted in three siblings and no other relatives.<sup>3</sup> Two authors have recorded cases in which four siblings were affected.<sup>4</sup> In one family the condition was found in two brothers and their two first cousins,<sup>5</sup> and in another family, in three brothers and their two first cousins.<sup>6</sup>

From the Department of Dermatology and Syphilology, Cleveland City Hospital, Harold N. Cole, Director

1 (a) Mackenzie. *Tr. Path. Soc. London* **33** 370, 1882. (b) Startin *ibid.* **33** 373, 1882. (c) Ehrmann. *Beitr. z. klin. Chir.* **4** 341, 1889. (d) Lehzen and Knauss. *Virchows Arch. f. path. Anat.* **116** 84, 1889. (e) Thiberge. *Ann. de dermat. et syph.* **5** 318, 1894. (f) Leskien. *Inaug. Dissert.*, Leipzig, 1903. (g) Gwynne. *Rep. Soc. Study Dis. Child.* **5** 318, 1905. (h) Arning. *Arch. f. Dermat. u. Syph.* **105** 290, 1910. (i) Linser. *München med. Wchnschr.* **67** 85, 1920. (j) Beeson, B. B., and Albrecht, P. G. *Contribution to Study of Xanthoma Tuberosum*, *Arch. Dermat. & Syph.* **8** 695 (Nov.) 1923. (k) Pautrier and Levy. *Presse med.* **31** 728, 1923. (l) Gordon and Feldman. *J. Michigan M. Soc.* **23** 231, 1924. (m) Gilbert, Chabrol and Benard. *Bull. et mem. Soc. med. d. hop. de Paris* **22** 1067, 1926. (n) Wile, U. J. and Duemling, W. W. *Familial Xanthoma*, *Arch. Dermat. & Syph.* **21** 642 (April) 1930. (o) Hufschmitt and Nessman. *Ann. de dermat. et syph.* **1** 462, 1930. (p) Van den Bergh, A. A. H., and Jordans, G. H. W., in *Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman*, New York, International Press, 1932, vol. 3, p. 1151. (q) Lane, C. Guy and Goodman, Joseph, Jr. *Xanthoma Tuberosum*, *Arch. Dermat. & Syph.* **32** 377 (Sept.) 1935.

2 Startin<sup>1b</sup> Ehrmann<sup>1c</sup> Lehzen and Knauss<sup>1d</sup> Thiberge<sup>1e</sup> Gwynne<sup>1g</sup> Wile and Duemling<sup>1n</sup>

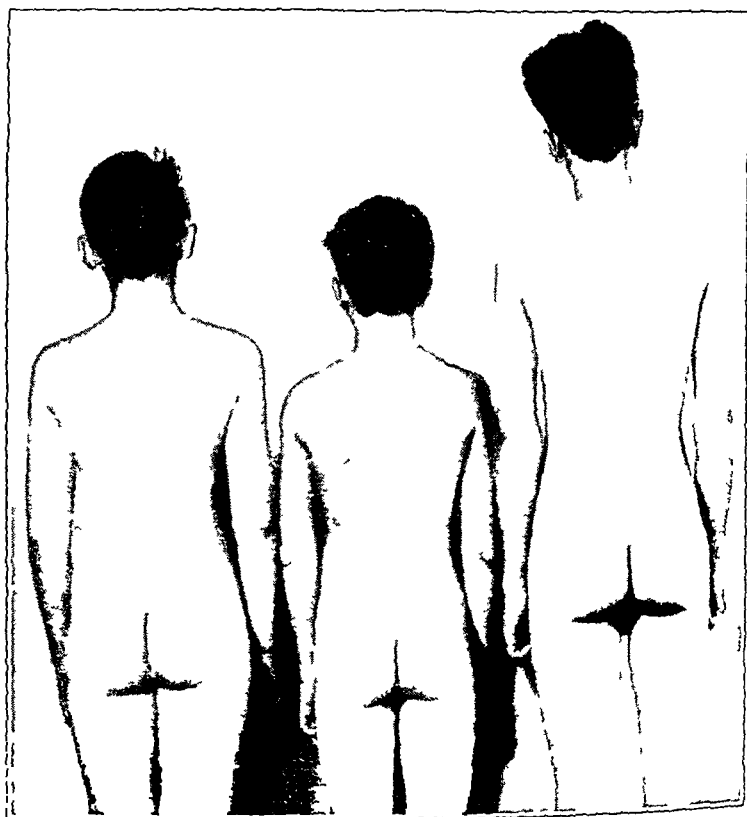
3 Leskien<sup>1f</sup> Pautrier and Levy<sup>1k</sup>

4 Linser<sup>1i</sup> Hufschmitt and Nessman<sup>1o</sup>

5 Van den Bergh and Jordans<sup>1p</sup>

6 Gilbert, Chabrol and Benard<sup>1m</sup>

There are three reports of xanthoma in two generations, the first was that of a mother and four children,<sup>7</sup> the second that of a mother and three sons<sup>8</sup> and the third that of a mother and one son.<sup>9</sup> Most interesting is the first mention in the literature of familial xanthoma which includes members of the first and the third generation but not the second generation, namely, the report of the condition in two brothers and a sister and paternal grandfather. To these is added the following report



Photograph of the patients, showing xanthoma. Note the lesions on the elbows of two of the patients and the lesions on the buttocks of two.

#### REPORT OF CASE

Three apparently healthy white boys, brothers, 12, 13 and 15 years old, respectively, were brought to the clinic by their father to have some yellowish tumor masses removed. There were two other siblings—a boy and a girl—but they were not similarly affected. No other members on either side of the family were known to have had any tumor masses resembling these, and there was a com-

7 Arning<sup>11</sup>

8 Beeson and Albrecht<sup>11</sup>

9 Gordon and Feldman<sup>11</sup>

pletely negative history of tumor throughout three generations. The past histories of the boys were uneventful. Each had had measles, mumps and pertussis, but no other illnesses and no operations. With the exception of the cutaneous findings nothing abnormal or remarkable was found on complete physical, ophthalmoscopic and fluoroscopic examination.

Studies of the blood lipids<sup>10</sup> showed the data given in the table, allowing for normal persons 0.18 Gm. of cholesterol per hundred cubic centimeters of blood plasma, 0.2 Gm. of lecithin and 0.8 Gm. of total fat.

In these patients urinalyses and Wassermann tests of the blood gave negative results. The blood picture was normal in the 13 year old boy, but showed a basophil count of 6 per cent in the 12 year old boy and of 20 per cent in the 15 year old boy. In each case the urea nitrogen, blood sugar during fasting, sugar

*Cholesterol, Lecithin and Total Lipoid Values per Hundred Cubic Centimeters of Blood Plasma for the Three Patients*

Patient	Age, Years	Date	Cholesterol, Gm.	Lecithin, Gm.	Total Fat, Gm.
D. R.	12	June 25	0.438		
		June 28	0.443		
		July 7	0.483		
		July 12	0.428		
		July 17	0.460	0.670	2.08
R. R.	13	July 12	0.390		
		July 17	0.467	0.642	2.76
E. R.	15	July 10	0.480		
		July 12	0.425		
		July 17	0.409	0.589	2.42

tolerance reaction and basal metabolic rate were within normal limits. Biopsies in all three instances showed a typical histopathologic picture of xanthoma.

#### CONCLUSIONS

There are added to the literature on familial xanthomatosis reports of the cases of three of five siblings with xanthoma tuberosum multiplex.

The family history on both sides was negative for xanthoma.

The blood pictures of two of the patients showed the percentage of basophils to be markedly increased.

In all three patients the values for cholesterol, lecithin and total lipid were abnormally increased.

<sup>10</sup> The determinations were made by Dr. Ramon F. Hanzal, Department of Biochemistry, Western Reserve University.

# AMYLOIDOSIS CUTIS LICHENOIDES

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AND

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It is only recently that a report of a case of localized cutaneous amyloidosis appeared in the American dermatologic literature, although this condition has been familiar to European writers for about fifteen years. In Germany and Italy, Juliusberg, Koenigstein, Gutmann, Sannicandio and others have reported more than thirty cases, and it is probable that it occurs with equal frequency in this country but has escaped general recognition.

Virchow named the substance occurring in this condition amyloid because of the starchlike reaction which usually resulted when the lesions were treated with aqueous solution of iodine and dilute sulfuric acid. Bonetus<sup>1</sup> in the seventeenth century referred to the homogeneous, glassy substance as wooden induration. From Rokitansky came the designation lardaceous degeneration.

Kekule<sup>1</sup> (1858) and Friedreich<sup>2</sup> classified amyloid substance with the group of albuminoids. This classification Schmidt confirmed in the following year. A step forward resulted from the work of Krawkow, who regarded the substance as a combination of albumin and chondroitin and sulfuric acid. Although this chemical conception has found its way to modern textbooks, Lubarsch<sup>3</sup> stated that there are unclear and disputed points that need elucidation. Eppinger<sup>4</sup> working with masses of pure amyloid, failed to recover sulfur, phosphorus or carbohydrate. The substance differs in many respects from hyalin, with which it is confused. The latter is a variable substance

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Read before the regular monthly conference of the staff at the sanatorium of the Jewish Consumptives' Relief Society, Spivak, Colo., May 8, 1935.

1 Kekule, cited by Trambusti, A. *Patologia della cellula* in For. Pio. Trattato di anatomia patologica per medici e studenti, Torino, Italy, Unione tipografica editrice Torinese, 1922, p. 117.

2 Friedreich, in Ribbert, M. W. H. *Lehrbuch der allgemeinen Pathologie und der pathologischen Anatomie*, Leipzig, F. C. W. Vogel, 1908, p. 115.

3 Lubarsch, O. *Die hyalinen und amyloiden Ablagerungen* in Henke, F. and Lubarsch, O. *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1926, vol. 1, p. 459.

4 Eppinger cited by Wallace, J. E. *Diagnosis of Amyloid Disease* *Lancet* 1: 391 (Feb. 20) 1932.

chemically and morphologically and as to origin. It has a tendency to stain with acid aniline dyes, while amyloid reacts characteristically to methyl green and methyl violet.

It was first pointed out by Heschl<sup>5</sup> (1879) that methyl green is the reagent for amyloid. His observations were confirmed by Curschmann (1880), who showed that it stains amyloid an intense violet. It is known that good results can be obtained with Cornil's method, using tissue fixed with a solution of formaldehyde.

Amyloid has a marked affinity for congo red. Congo red cannot be used with tissue fixed with a solution of formaldehyde, as the color will be lost. The injection of congo red intravenously to stain amyloid was suggested by Bennhold<sup>6</sup> in 1923. The amount of dye recovered from the plasma is an index of the extent of lardaceous degeneration, and it has recently been shown that congo red injected subcutaneously beneath the lesions will find its way to amyloid deposits in the conium.

#### REPORT OF A CASE

H. L., a writer aged 47, from the Sanatorium of the Jewish Consumptives' Relief Society, was first seen in the hospital service of Dr. A. J. Markley on Feb. 20, 1935, with a complaint of an itchy eruption on his legs. No diagnosis was made on this visit, and the patient was requested to return for further study. On his second visit he gave the following history:

The family history was irrelevant except for the fact that his father had had an itchy condition of the legs for many years. The patient went to school until 16 years of age and then became a teacher. He was in prison in Siberia for seven years and came to America in 1913. There was a past history of typhus in 1910, Vincent's angina in 1911 and influenza in 1912. The patient was of the opinion that his lungs were affected at the time of the attack of influenza. He had furunculosis from 1929 to 1932. He stated that he had not had a venereal disease. He had had no injuries or operations.

The patient dated the onset of pulmonary tuberculosis from October 1922, when he began to notice cough and expectoration, increased pulse rate and subfebrile temperature. A diagnosis of pulmonary tuberculosis was made at that time, and after a rest of one year he returned to his work. He tired easily, coughed and was very susceptible to colds. In 1932 he began to suffer from chills, night sweats and increased cough and expectoration, and at that time he came to the sanatorium of the Jewish Consumptives' Relief Society. The clinical course of the patient in the sanatorium was uneventful, and the condition was diagnosed as far advanced tuberculosis of both lungs. Roentgen diagnosis confirmed the physical findings of far advanced chronic fibrocavernous tuberculosis, with slight activity in the upper lobe of the right lung. The patient was ambulant and afebrile, and the symptoms were practically nil. Examination of the sputum gave negative results. His only complaint was frequency of urination, associated with occasional pain, and

<sup>5</sup> Heschl cited by Lee, A. B. *Microtome's Vade-Mecum*. Philadelphia: P. Blakiston's Son & Co., 1905, p. 197.

<sup>6</sup> Bennhold, H. Ueber die Ausscheidung intravenos eingegebenen Kongorotes bei den verschiedensten Erkrankungen insbesondere bei Amyloidose. *Deutsches Arch. f. klin. Med.* **142**: 32, 1923.



for this prostatic massage was given. After residence of six and one-half months he left the sanatorium, with the tuberculous lesions quiescent and with the prognosis favorable. After he was discharged the patient stayed in New York for one and one-half years, at the end of which time he felt worse. He therefore returned to Spivak, Colo., on Sept 6, 1934. Examination revealed no change in his general condition and that of his chest. There was a moderate dry cough but no expectoration, and the disturbances of urination had subsided completely. The patient was ambulant and afebrile. He stated that he had suffered from itching all over the body all his life. During the past five years the itching had



Fig 1—The anterior surface of the legs on which the majority of lesions are located

become worse and had concentrated especially on both legs. Two years previously a papular eruption developed on both lower extremities, which started with the ankles and progressed toward the hips.

*Laboratory Observations*—The sputum could not be examined because there was no expectoration. The sedimentation rate was 3 mm the first hour and 9.5 mm the second hour. The vital capacity was 121 per cent. The red blood cell count was 4,700,000, the white blood cell count was 7,900, the hemoglobin content was 80 per cent and the color index was 0.8. The differential count was segmented forms 60 per cent, lymphocytes 33 per cent, monocytes 1 per cent, staff

cells 4 per cent, and eosinophils 2 per cent. Examination of the urine gave negative results. The reaction to the Wassermann test was negative.

*Dermatologic Examination (O S P)*—There were no cutaneous abnormalities other than a papular eruption of the legs of about two years' duration. This eruption (fig 1) was symmetrically distributed, and the lesions were more abundant on the flexor than on the extensor surfaces. On the ankles the lesions were closer together, larger and more numerous than elsewhere. It was here that the condi-

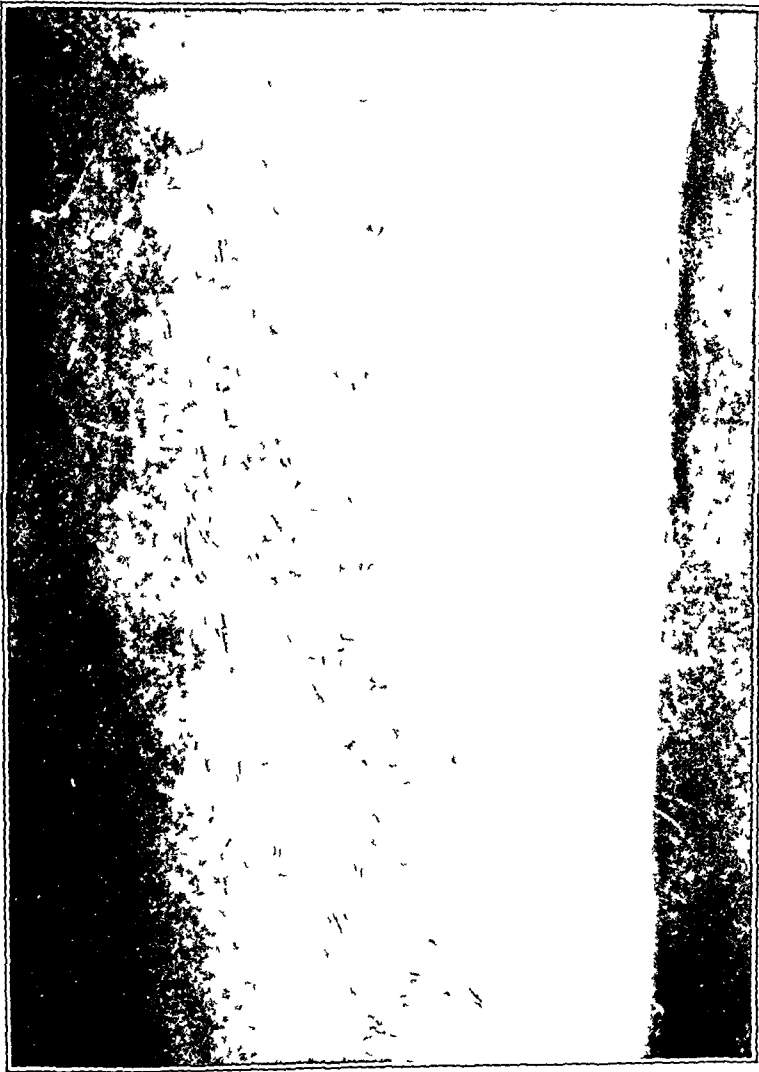


Fig 2—The flexor surface of the legs showing papular lesions—some verrucous, some crusted and occasionally one with a hair protruding through the top.

tion first appeared, gradually spreading upward, the most recent lesions appearing as papules the size of a pinhead on the knees. The eruption was entirely papular, although some lesions appearing to be vesicular or slightly translucent were firm and hard. They were faintly yellow, some being slightly pink or reddish brown. They varied from the size of a pinhead to that of a matchhead and were conical or hemispherical. Many were capped (fig 2) with a verrucous scale, and on others such scales had been removed or replaced by bloody crusts as the result of scratching. A few lesions formed in the follicular orifices and through each of these a hair protruded.

*Diagnosis*—The conditions considered in the diagnosis were lichen planus, lichen simplex chronica, verruca vulgaris, Darier's disease, pityriasis rubra pilaris and molluscum contagiosum

Study of the material taken for biopsy, however, at once excluded all the possibilities. The sections presented unusual features, evidently the result of an infiltrative process. Search of the literature for analogous conditions disclosed reports<sup>7</sup> of two cases of localized cutaneous amyloidosis in which the clinical and microscopic observations were practically identical with those in the present case. After this by special staining methods, the diagnosis of the condition was made. The subcutaneous injection of congo red beneath several typical lesions, as recently suggested by Nomland,<sup>8</sup> resulted in their being stained a bright red which persisted for several weeks. Bennhold's intravenous test with congo red revealed a 29 per cent decrease after one hour, indicating the absence of amyloid

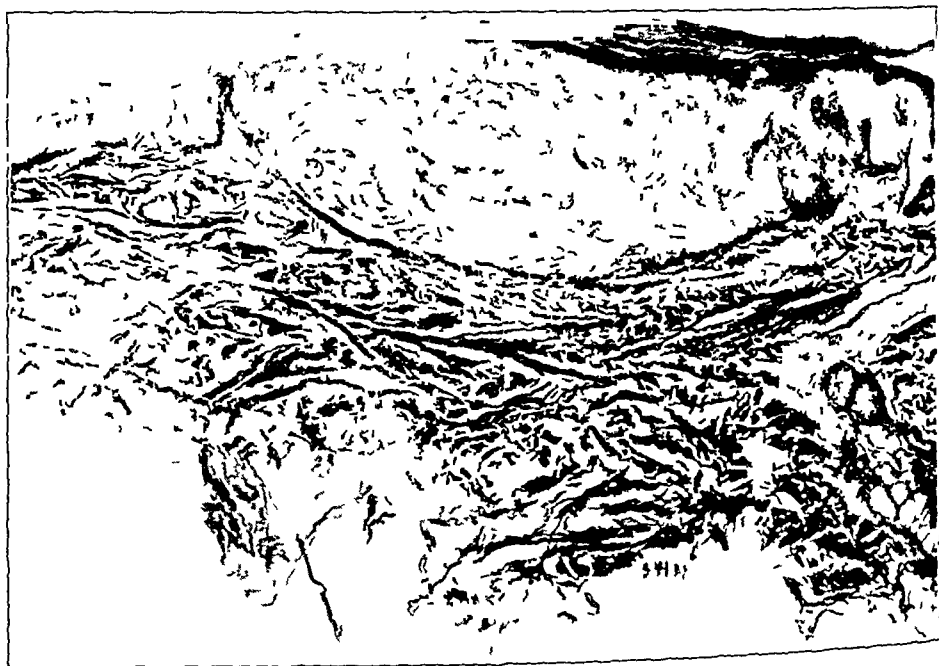


Fig 3—A photomicrograph ( $\times 40$ ) of a frozen section fixed in a solution of formaldehyde and stained with hematoxylin and eosin. It shows atrophy of the epidermis and disappearance of the rete ridges. Hyperkeratosis is present. The amyloid nodule is seen beneath the epidermis in the papillary bodies.

temic amyloidosis, since it has been demonstrated that amyloid deposited in the skin does not absorb the dye when it is administered intravenously.

*Histopathologic Picture of the Cutaneous Lesions* (A. W. F.)—Frozen sections stained with hematoxylin and eosin (fig 3) revealed large nodular masses consisting of broad wavy bundles of homogeneous-staining material, poor in cellular elements.

7 Winer, L. H. Local Amyloidosis of the Skin, Arch Dermat & Syph. 23: 866 (May) 1931. Ormsby, O. S. Diseases of the Skin, ed. 4, Philadelphia: Lea & Febiger, 1934, p. 672.

8 Nomland, R. Localized (Lichen) Amyloidosis of the Skin, Arch Dermat & Syph. 33: 85 (Jan) 1936.

ments, beneath the epidermis. The rete cones had disappeared. There was a thinning of the horny layer overlying the lesion. Other areas showed well developed papillary bodies, with smaller nodules separated by well developed rete cones. The homogeneous material was deposited about the thin-walled capillaries in the papillary bodies. In the upper layer of the cutis was moderate round cell infiltration.

Sections stained with orcein (Grubler's) showed absence of elastic fibers in and about the homogeneous areas.

Unfixed frozen sections stained with methyl violet showed the nodules in the corium to be deep red, the surrounding tissue was blue.

Sections (fig 4) treated with aqueous solution of iodine U S P showed the nodules to be a mahogany color, which changed to light blue, or grayish blue, when washed in dilute sulfuric acid.

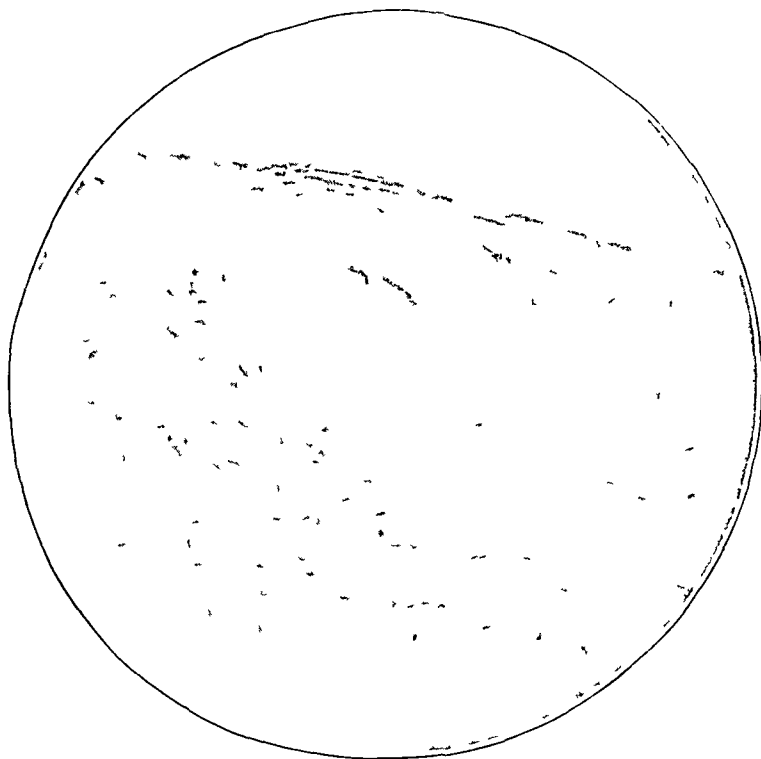


Fig 4—Photomicrograph of an unfixed frozen section stained with iodine. It demonstrates the amyloid nodule in the papillary bodies, with thinning of the epidermis and disappearance of the rete cones.

A subcutaneous injection of 1 cc of a 1 per cent solution of congo red was made beneath two lesions, and microscopic examination of unfixed material from these lesions forty-eight hours later revealed the amyloid substance in the corium to be stained light red, with the surrounding tissue colorless.

#### COMMENT

This case demonstrates the difficulty of proving by routine staining methods a clinical diagnosis of amyloidosis cutis, and it emphasizes the need for further investigation into the nature of amyloid, particularly in regard to its reactions to stains. It demonstrates further the need

for persistent and repeated attempts to prove the presence of amyloid, even after one or two apparent failures. The results reported in the literature and in the present case prove that an examination in a suspected case of amyloidosis cutis is not complete unless numerous staining methods are tried and then results are reported.

#### SUMMARY

A case of amyloidosis cutis lichenoides has been reported in a man who had pulmonary tuberculosis for many years.

A section of fixed tissue stained by routine methods failed to demonstrate conclusively the presence of amyloid, but tissue treated by the methods outlined in this paper gave definite and positive evidence of its presence.

A subcutaneous injection of congo red gave a positive vital stain to the lesions, even after the disappearance of the rosy-hued congo red stain in the surrounding skin.

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# SPHACELODERMA

## REPORT OF A CASE OF UNUSUAL PHAGEDENIC ULCERATION OF THE SKIN SUBCUTANEOUS TISSUE AND MUSCLE OF THE CHEST WALL

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Gangrene of the skin<sup>1</sup> (sphaceloderma) may be single or multiple acute or chronic local or general (some types are peculiar to certain areas),- symmetrical or asymmetrical small or extensive. Gangrene may be a sequela to one of a variety of conditions, or it may be spontaneous.<sup>3</sup>

Crocker stated "Single gangrenous patches often of large size are met with in infants and young children both spontaneously and as a result of infectious fevers. They start as a vesicle, pustule or bulla."

Gangrenous lesions caused by the ingestion of iodides were reported by R. Parker in a girl aged 10 years and by Audrey in a woman aged 47. Wende reported a fatal case in which bullous lesions developed in a chronic ulcer on the leg. These subsequently became gangrenous. Streptococci, staphylococci, diplococci and bacilli were found in the bullae and in the gangrenous lesions during life and in the internal organs at autopsy. A case reported by Waelsch also proved fatal. After the use of a morphine syringe gangrenous patches and abscesses developed in a man aged 38. He died in three weeks. A bacillus was

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From the surgical division of Dr. Edgar Burke and from the dermatological department of Dr. Wilbert Sachs, Jersey City Medical Center.

1 Crocker, H. R. *Diseases of the Skin*, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903, p. 527. Stelwagon, H. W., and Gaskill, H. K. *Diseases of the Skin*, ed. 9, Philadelphia, W. B. Saunders Company, 1921, p. 427. Ormsby, O. S. *A Practical Treatise on Diseases of the Skin*, ed. 4, Philadelphia, Lea & Febiger, 1934, p. 356.

2 Hilbert, R. Spontaneous Gangrene of the Eyelids, *Vierteljahrsschrift für Dermat.* **11** 117, 1884. Corbus, B. C. Erosive and Gangrenous Balanitis, *J. A. M. A.* **60** 1769 (June 7) 1913. Gate, J., and Rousset, J. Gangrene of the External Genitalia Caused by *Spironema Vincentii*, *Ann. de dermat. et syph.* **10** 151 (Feb.) 1929. Palmer, H. E. Gangrenous Vulvitis or Noma Pudendi, *Florida M. A. J.* **16** 31 (July) 1929. Chevallier, P. D., Levy-Bruhl, M., and Moricard, R. Idiophagedena of the Vulva (Geometric Phagedena of Brocq and Simon), *Bull. Soc. franç. de dermat. et syph.* **38** 212 (Feb.) 1931. Peacock, S. C. Dry Gangrene of the Face, with Mummification and Separation *en Bloc* of the Nose and Adjacent Tissues, *Am. J. Dis. Child.* **45** 815 (April) 1933.

3 Smith, L. D. Spontaneous Gangrene of the Extremities, *Am. J. Dis. Child.* **44** 151 (July) 1932.

found that did not stain by Gram's method. A fatal case was reported by Lancashire. The condition involved the lower part of the abdomen, the inguinal regions and the inner surface of the upper part of the thighs. There was chronic eczema in the involved region. *Bacillus pyocyaneus* and *Staphylococcus aureus* were found. In a case reported by Hartzell, vaccinia-like lesions, later becoming gangrenous, developed in a woman, aged 46, after an injury with a poisoned meat-hook. In the bullae and in the sloughs from the gangrenous areas many bacilli and staphylococci (*Staph aureus*) were found. The case reported by Hallopeau started with acne-like papules, which quickly exfoliated leaving an ulcer. Gangrenous ulcers are usually small, but in the cases of most severe involvement they may slough and suppurate and extend over a large area. The condition occurs most frequently on the face, but it may affect mucous membranes and the mouth and even the chest and arms. All these cases were cited by Crocker.

Cases of extensive ulceration caused by amebas were reported by Engman and Heithaus, by Engman and Meleny and by Crawford.<sup>4</sup> In the first two cases the condition developed after incision of an amebic abscess and after a surgical intervention on the intestinal tract, respectively. In the case reported by Crawford it was associated with amebic colitis, but no surgical procedure was done. The condition starts as a very painful tender abscess which ruptures and discharges a thick pus. The edges become undermined, and about them there is a red areola. Amebas may be found in the wound and in the feces.

Dermatitis gangraenosum infantum,<sup>5</sup> or *ecthyma telébiante*, is a gangrenous eruption which follows varicella and other pustular eruptions and occasionally occurs spontaneously. Stelwagon stated that it occurs in patients under the age of 3 years, appearing most commonly in the first year. The condition starts as pinhead-sized papulopustular multiple lesions, which become crusted and beneath which ulceration begins. The process may extend peripherally, or lesions near each other may become confluent, and large areas may be involved. When the condition arises spontaneously it usually begins about the buttocks. Extensive lesions are usually associated with marked constitutional involvement (temperature 104 F, vomiting, etc.) and pulmonary and cardiac complications, and as a rule the termination is fatal. Mild lesions may have few concomitant symptoms.

<sup>4</sup> Engman, M. F. and Heithaus, A. S. Amebiasis Cutis, *J. Cutan. Dis.* **37** 715 (Nov.) 1919. Engman, Martin F., Jr., and Meleny, Henry E. Amebiasis Cutis (*Endamoeba histolytica*). Report of Two Cases, *Arch. Dermat. & Syph.* **24** 1 (Jul.) 1931. Crawford, Stanley. Amebiasis Cutis. Report of a Case *ibid.* **28** 363 (Sept.) 1933.

<sup>5</sup> Pasachoff, Harry D. and Sobel, Nathan. Dermatitis Gangraenosa Infantum in the Course of Scarlet Fever, *Arch. Dermat. & Syph.* **26** 428 (Sept.) 1932.

Cases of postoperative progressive gangrene were reported by Baker and Terry, Horsley, Cullen, Lynn, Freeman, Christopher, Bremer and Meleney, Ballin and Morse.<sup>6</sup> The ulceration usually follows operation starting around a stitch. The affected area becomes painful, swollen and purple and quickly ulcerates. This condition rapidly spreads. The subcutaneous fat, fascia and skin are involved. The temperature is only moderately elevated even when the wound is extensive. The etiologic factor in these cases is thought to be a symbiotic synergistic infection with two types of bacteria. A similar condition was described by Horsley,<sup>7</sup> which did not follow operation. However the patient had urinary disturbances, his condition was more toxic (vomiting, high pulse rate, some fever) than that noted in the other cases and the wound spread more rapidly.

Pyoderma gangraenosum, as described by Brunsting, Goeckerman and O'Leary, by McCarthy and Fields and by Lane and Stroud,<sup>8</sup> has a definite relationship with infections of long standing elsewhere in the body. There are improvement and recurrence, with similar changes in the general condition. The primary lesion is a papule or a small nodule, which becomes encrusted and ulcerated. The lesions are multiple and vary in diameter from 1 cm to 14 cm. *Staphylococcus albus* and a streptococcus were found in the lesions.

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6 Baker, W. H., and Terry, C. C. A Case of Postoperative Progressive Gangrene of the Skin, *J. A. M. A.* **98** 138 (Jan 9) 1932. Horsley, J. S. Intussusception Due to Intestinal Lipoma in an Adult, Followed by Gangrene in the Abdominal Wall, *Arch. Surg.* **18** 882 (March) 1929. Cullen, T. T. A Progressive Enlarging Ulcer of the Abdominal Wall Involving the Skin and Fat Following Drainage of an Abdominal Abscess, Apparently of Appendiceal Origin, *Surg., Gynec. & Obst.* **38** 579 (May) 1924. Lynn, F. S. Postoperative Gangrenous Ulcer of the Abdominal Wall, *J. A. M. A.* **97** 1579 (Nov 28) 1931. Freeman, Leonard. Progressive Gangrenous, Painful Ulceration of the Abdominal Skin and Subcutaneous Tissues Following Operation, *Ann. Surg.* **92** 779 (Oct) 1930. Christopher, F. Severe Spreading Carbuncular Infection of Chest Wall Following Rib Resection Under Local Anesthesia, *S. Clin. North America* **4** 795 (June) 1924. Bremer, G. E., and Meleney, Frank L. Progressive Gangrenous Infection of the Skin and Subcutaneous Tissues Following Operation for Acute Perforative Appendicitis, *Ann. Surg.* **84** 438 (Sept) 1926. Ballin, Max, and Morse, P. F. Progressive Postoperative Gangrene of the Skin, *Am. J. Surg.* **11** 81 (Jan) 1931.

7 Horsley, J. Shelton. Certain Symbiotic Bacterial Infections Producing Gangrene, with Special Reference to the Principles of Treatment, *J. A. M. A.* **98** 1425 (April 23) 1932.

8 Brunsting, L. A., Goeckerman, W. H., and O'Leary, Paul A. Pyoderma (Ecthyma) Gangraenosum. Clinical and Experimental Observations in Five Cases Occurring in Adults, *Arch. Dermat. & Syph.* **22** 655 (Oct) 1930. McCarthy, Lee, and Fields, Russel. Pyoderma Gangraenosum, *New York State J. Med.* **31** 801 (July 1) 1931. Lane, Clinton W., and Stroud, Malone C. Pyoderma Gangraenosum. Report of Case, *Arch. Dermat. & Syph.* **27** 460 (March) 1933.



Nocardiosis cutis gangraenosa was described by Guy and Helmbold.<sup>9</sup> The patient had a septic temperature and bloody dysentery. The lesions were multiple and very painful. With the appearance of the lesions the patient had a rise in temperature, chills, nausea, anorexia and general symptoms of an acute infection. To a great extent the condition is similar to pyoderma gangraenosum, except that the organism *Nocardia* was recovered from the lesions. Gangrene due to hemolytic streptococci follows a cutaneous wound, gangrene occurring several days after the injury and spreading rapidly to include the subcutaneous tissue. This has been described by Meleney, Jen, Bates and Fallon.<sup>10</sup>

#### REPORT OF CASE

M. M., a girl aged 10 years, born in New Jersey of Polish parentage, was well, aside from having had measles and an occasional cold, up to the onset of the condition described in this paper. Her parents, brothers and sisters were living and well. There was no history of tuberculosis, diabetes or syphilis in the family.

During January 1931 she was treated at the Jersey City Medical Center in the outpatient department of the surgical division for a "furuncle" of the left axilla. This was incised and found to be purulent, several days later the lesion became necrotic and began to slough. During February 1931 a superficial fluctuating area developed left of the sternum at the level of the second and third ribs. This was incised and drained and, like the axillary lesion, in a few days became necrotic and began to slough and to extend peripherally.

The patient was admitted to the hospital on March 17, 1931. At that time there were two ulcerated areas, one covered the entire medial surface of the left arm to within 2 inches (5 cm) of the cubital fossa and extended over the entire left axilla and the lateral surface of the chest almost down to the twelfth rib, the other extended from the left margin of the sternum up to the midaxillary line. The two ulcerated areas were separated by a 1 inch (2.5 cm) strip of undermined skin. The base of the ulcer showed a red granulating surface with some purulent secretion and in places the pulsations of the heart were clearly visible. The margins were undermined, and the skin and subcutaneous tissue were raised off the muscle, with purulent necrotic material between (fig. 1).

The general condition of the patient was good and continued so with the exception that her temperature at all times ranged between 99 and 100 F. She was confined to bed, with her arm raised in a splint in the attempt to avoid a contracture between the arm and the chest wall, but later, when she was allowed to be up her appetite and color improved. (During an epidemic of diphtheria in the ward she contracted the disease but recovered rapidly.)

9. Guy, W. H. and Helmbold, T. R. Nocardiosis Cutis Gangraenosa, Arch Dermat & Syph **27** 224 (Feb) 1933.

10. Meleney, Frank L. Hemolytic Streptococcus Gangrene Arch Surg **9** 317 (Sept) 1924. Jen, T. K. Hemolytic Streptococcus Gangrene, China M J **43** 889 (Sept) 1929. Bates, John T. Subcutaneous Streptococcus Gangrene, Ann Surg **90** 1029 (Dec) 1929. Fallon, John. Hemolytic Streptococci Subcutaneous Gangrene. Report of Case Arch Surg **18** 1817 (April) 1929.

*Laboratory Examination*—All tests were repeated several times. The Wassermann reaction of the blood was negative. Blood counts showed from 15,000 to 17,000 white cells and from 3,000,000 to 4,000,000 red cells. The hemoglobin content was from 40 to 50 per cent, and the color index was 0.6. The sputum was normal at all times, and the throat was normal except when the patient had diphtheria. There were no gonococci. The stools contained no amebas. No reaction was obtained when a guinea-pig was inoculated. A smear of material from the wound contained no tubercle bacilli, amebas or fusiform bacilli. Staphylococci but no fungi could be cultured. Biopsy disclosed granulation tissue, which was of no special type.

Roentgenograms showed nothing abnormal, except that on Jan. 25, 1932, there was a trophic condition of the bones of the shoulder, the humerus and the upper part of the radius and ulna. There was a proliferative process of the inner aspect of the shaft of the humerus from the surgical neck downward about 2 inches (5 cm). On June 6, 1932, the chest showed a generalized infiltration throughout



Fig 1—Photograph of the patient at about the time of admission to the hospital

the entire right lung and the upper lobe of the left lung, which was suggestive of infection with the tubercle bacillus. There was osteomyelitis, involving the upper half of the left humerus.

*Therapy*—Hydrogen peroxide, physiologic solution of sodium chloride, hypertonic solutions of sodium chloride up to 10 per cent and bacteriophage were used as wet dressings at various times, each being given a fair trial period. The edges of the lesion were painted with silver nitrate at first, later pure lactic acid was used. From May 1931 to February 1932, she was exposed to radiation from a carbon arc lamp three times a week for twenty minutes at each sitting. At the same time she was exposed to the sun's rays daily. She was given eight injections of antimony and potassium tartrate to rule out amebiasis and leishmaniasis. She received a high caloric diet, viosterol, beef hemoglobin and liver extract in an alcoholic menstruum, iron and ammonium citrate, potassium iodide, solution of potassium arsenite and solution of iron and ammonium acetate. One blood transfusion of 300 cc. was given in the attempt to improve her resistance.

*Subsequent History*—The patient's general condition remained good throughout. The osteomyelitis of the left humerus became progressively worse, and on Dec 15, 1932, the area was operated on, and the necrotic granulations were curetted. She responded well to this, and the condition gradually improved.

The wound remained more or less stationary during 1933 and 1934, with the occasional appearance of healthy granulations at several points. In December 1934 she went home for two weeks for the Christmas holidays. She returned to the hospital, and since that time the wound has slowly but progressively improved, until at the time of writing the entire area has undergone epidermizations.

The treatment was continued throughout the entire time as at the start, the use of each of the various remedies was repeated many times. At no time before or during the healing was any special treatment used.



Fig 2—Photograph of the patient after the lesions had healed, showing the extent of the scar formation.

All the laboratory examinations were repeated too often to tabulate. She received three blood transfusions: 300 cc on Aug 1, 1932, and, Nov 30, 1932, and 350 cc on Dec 16, 1932.

*Condition at the Time of This Report*—The girl is 14½ years old, is well nourished and weighs 109 pounds (99 Kg). The osteomyelitis is completely healed. She has no subjective symptoms and, other than some impairment in motion, experiences no discomfort. There remains only a little motion in the left arm owing to adhesions to the chest wall. The left forearm has about 50 per cent motion, and there is full use of the left hand.

The left breast is gone. The right breast is present, but there are only the nipple and a small portion of the tissue of the breast about it. The outer portion of the breast is wanting. On lateral view, there is a marked concavity of the left side of the chest, causing considerable deformity of the thorax. The previously ulcerated areas are entirely healed. The scar extends across the whole wall of

the chest, the upper margin reaching to the top of the sternum in the center and on the sides and extending over the shoulders, the lower border reaches to the bottom of the chest wall. The scar extends down over the upper third of the right arm, on the left side it extends around the back, in the upper part to within 2 inches (5 cm) of the spine and in the lower part to the lower pole of the scapula. Almost the entire left arm is covered by the scar tissue. The edges of the scar are irregular, in places white smooth and at the same level with the surrounding skin and in places raised, well defined and red. The surface is in part smooth except for a few cordlike red bands traversing it in different directions. In the region of the left shoulder and left arm the surface is very irregular, with large masses protruding. There are large fibrous bands connecting the left side of the chest wall and the upper half of the left arm. In part the scar is smooth, stretched, thin and glossy in part it is wrinkled, dull and not unlike cigaret paper in appearance. Over the lateral surface of the left arm is a deep scar where the incision was made because of the osteomyelitis (fig 2).

#### NOTES ON PRESENTATION AND DISCUSSION OF THE CASE

This patient was presented by Dr. David Satenstein with a diagnosis of phagedenic ulcer at the October 1931 meeting of the Manhattan Dermatological Society.<sup>11</sup> Later in the same month the patient was presented by me for diagnosis at the Bronx Dermatological Society.<sup>12</sup> In January 1934 the patient was again presented by Dr. Satenstein and me at the Manhattan Dermatological Society.<sup>1</sup>

The discussions were directed chiefly toward therapy, no diagnosis was made but the following were suggested: tuberculosis, syphilis, severe scrofuloderma and *ecthyma telébrant*.

Similar cases had been observed by several of the men, in none was a diagnosis made, and none of them appear to have been reported.

Dr. Isadore Rosen stated: "I have seen two similar cases during the past few years, in which all the pathologic and bacteriologic studies failed to reveal a definite etiologic factor."

Dr. N. Sobel said: "I was fortunate enough to see a case similar to this in Jadassohn's Clinic about two years ago. The lesions were smaller, and the duration was over one year. Repeated examinations, carefully made, gave absolutely negative results, and no diagnosis could be made."

Dr. Ludwig Oulmann commented: "I saw a patient with a similar condition, who had fistulas and a rolling up of the epidermis, denuding the arm from the axilla to the wrist. The patient was tuberculous."

<sup>11</sup> Satenstein, D. Phagedenic Ulcer, Arch. Dermat. & Syph. **25** 390 (Feb) 1932.

<sup>12</sup> Sachs, W. A Case for Diagnosis, Arch. Dermat. & Syph. **25** 399 (Feb) 1932.

<sup>13</sup> Satenstein, D., and Sachs, W. Phagedenic Ulcer of Unknown Origin, Arch. Dermat. & Syph. **30** 156 (July) 1934.

Morrow,<sup>14</sup> in discussing a case of dermatitis gangraenosa chronica presented at a meeting of the San Francisco Dermatological Society mentioned several cases of a condition which corresponded closely to the one reported here

Y Tsutsui<sup>15</sup> reported the case of a man who had a large chronic progressive gangrenous lesion involving the entire anterior wall of the chest, the axillae and the upper portion of the abdomen

#### DIFFERENTIAL DIAGNOSIS

The history, clinical picture and course and laboratory findings rule out extensive ulcerations caused by tuberculosis, syphilis, actinomycosis blastomycosis, sporotrichosis and coccidioidal granuloma

Never was there any history of ingestion of drugs, especially iodides before admission to the hospital. The clinical appearance and the pathologic findings were against the diagnosis of the condition as an eruption caused by drugs. The wound healed, even though the patient was taking iodides.

The cases reported by Wende, Waelsch and Lancashire were fatal, in all there was a preexisting condition, the progress was rapid and organisms were recovered. The case reported by Hartzell followed an injury, the lesions were multiple, and organisms were found. The acne-like multiple lesions, location, duration and course are unlike those in the case reported by Hallopeau.

Amoebiasis cutis is easily ruled out because in this disease there is either an operation or a condition harboring amebas or amebas are found in the stool. Besides, antimony and potassium tartrate was given to this patient as a therapeutic test with no results.

Dermatitis gangraenosa infantum is rarely extensive, localized and arising spontaneously. It occurs before the age of 3 years, usually first about the buttock, when not preceded by a pustular eruption, and when extensive it is accompanied by marked constitutional involvement and pulmonary and cardiac complications and is nearly always fatal. None of these features fit in with the condition in this case.

The condition in this case does not fit in with those of postoperative progressive gangrene and gangrene due to hemolytic streptococci because there was no operative intervention, the primary lesion was painful and ulcerated and extended extremely slowly and similar organisms were not found. In the case reported by Horsley there

14 Morrow Howard, in discussion on Templeton, H. J. Dermatitis Gangraenosa Chronica Arch Dermat & Syph 26 361 (Aug) 1932

15 Tsutsui Y. Ein Fall von seltener chronischer progressiver Hautgangrän Arch f Dermat u Syph 85 219, 1907

were toxic manifestations and constitutional disturbance (urinary), and the wound spread rapidly

Pyoderma gangraenosum is also associated with constitutional symptoms, the lesions are multiple and the primary lesion is a papule or a small nodule. The patients are toxic at times. The largest lesions are small compared with the one in the present case. Besides, similar organisms were not found.

The condition in this case is not like those described as nocardiosis cutis gangraenosa for the same reasons given in regard to pyoderma gangraenosum. Nocardia was not found.

#### COMMENT

From the foregoing data it can easily be seen that the condition in the case reported does not fit in with any of the types of gangrene described. It belongs to an undiagnosed or unclassified type of gangrene mentioned by Crocker in his textbook and by Rosen, Sobel and Oulmann in a discussion of this case and is similar to a type of cases which have been presented at meetings of various dermatologic societies. In order to summarize the many different types of gangrene the following classification is suggested:

- I Caused by obstruction of circulation
  - (a) Embolism and thrombosis within vessels
  - (b) Changes in wall produced by
    - 1 Acute arteritis—bacterial, syphilitic
    - 2 Degeneration—senile gangrene, decubitus
    - 3 Physical agents—heat, cold, radiation
    - 4 Chemical and medicinal agents—caustics, acids, alkalis, ergot, and iodides
  - (c) Pressure on vessels from without owing to inflammation, effusion, extravasation of blood, scars and tumors
- II Associated with acute inflammatory disease
  - (a) Typhoid, malaria, pneumonia, scarlet fever and erythema multiforme
- III Associated with chronic systemic disease
  - (a) Leprosy, tuberculosis, syphilis and diabetes
  - (b) Debilitating disease—cardiac, pulmonary, hepatic, renal
  - (c) Gastro-intestinal diseases (especially of the colon) diseases of the blood and neoplasms
- IV Associated with nervous disorders
  - (a) Raynaud's disease, hysterical gangrene and syringomyelia (Morvan's disease)

## V Caused by micro-organisms

- (a) Noma, dermatitis gangraenosa infantum, gas gangrene, gangrene due to hemolytic streptococci, gangrene from symbiotic bacterial infections, postoperative progressive gangrene, tropical phagedena (?) pyoderma gangraenosum, nocardiosis cutis gangraenosa, traumatic gangrene, actinomycosis, blastomycosis, sporotrichosis, granuloma coccidioides

## VI Unclassified

## SUMMARY

A case of extensive ulceration, of spontaneous origin, in a girl aged 10 years, showing no subjective or constitutional symptoms at any time, is reported. A diagnosis has not been made, and the condition is not like that in any case which has been reported. All laboratory investigation proved of little value, and the condition resisted all types of treatment. It started without any known cause and terminated after four years without apparent cause.

All the laboratory work was done in the laboratory of the Jersey City Medical Center

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# THE FIELD OF DERMATOLOGY

## PRESIDENT'S ADDRESS

WILLIAM ALLEN PUSEY, M D

CHICAGO

Skin diseases occur on the surface of the body, where every one can see them, and few recognize them. Because of the first fact and regardless of the second, most physicians are inclined to attempt to treat them. The result is that the dermatologist is inclined to think that the field that he should regard as his is a free-for-all domain, and in a sense it is. There is never a time when one group or another is not undertaking to appropriate some part of it. Every one comes forward with new suggestions, usually therapeutic for what he thinks is eczema, psoriasis, lichen planus, acne or what-have-you.

Now it is an internist, with a leaning toward intestinal disorders, who tells dermatologists how to treat cutaneous diseases by feeding the patient, or not feeding him, or by feeding him certain things. Give more sugar or give less, cut down the amount of protein or increase it, have him live on vegetables or some kind of hay. It is gout or rheumatism that is causing the trouble, or acidosis or alkalosis. Have him walk 3 miles a day in the open air, even if his feet do hurt from ringworm. Give him salicylates, arsenic, mercury cod liver oil, vitamin D, alkalis, acids, spinach or liver, discontinue cow's milk and give him goat's milk. Starve him or stuff him. Wash out his stomach or fill him with drugs. One's style is not cramped much when one is treating hypothetic causes of diseases which one does not know by methods which one likes to use.

Again, it is the allergists who think that they are the persons to treat skin diseases, even if they cannot recognize them, because they alone know how to make patch tests, scratch tests and intradermal tests, overlooking the fact that Jadassohn, a dermatologist, initiated the whole subject by introducing the patch test in 1895, that he and his pupil Bruno Bloch, another dermatologist, developed its precise application, and that they and other dermatologists following them not only have shown its value in an important group of dermatoses but have had perhaps a larger part than any one else in indicating the importance of allergy in general pathology. The allergists busy themselves in making patch tests with innumerable substances for lichen planus, lupus,



psoriasis, scabies chickenpox and syphilitic eruptions and finding causes that do not exist for these and other diseases that they do not know and on the basis of their findings treating the diseases by methods that do no good. One of the difficulties is, as I once heard a puzzled physician explain, that the skin tests show that the patient is sensitized to coca cola while sarsaparilla produces his hives. The allergists have a large field because their domain is the unknown, at least the unknown to them in dermatology. Seriously, I believe that it is the experience of dermatologists that they are likely to get no help from the allergists, even when they try to work in the closest cooperation. Their technic with cutaneous diseases does not give the satisfactory findings that the dermatologists get from their own technic, and their interpretations of the results are not borne out in the dermatologists' experience. It is like trying to be useful in finding something with the appearance of which one is unfamiliar in a strange room in the dark.

The roentgenologists and the radiologists would appropriate a large part of dermatology because they are so expert in handling the necessary machinery, overlooking the fact that the dermatologists have been expert enough to do practically all the original work in developing the therapeutic possibilities and uses of the roentgen rays and radium, that their work with skin diseases pointed the way to the therapeutic application of these agents for diseases of other structures and that they even did a great deal of the original work in the treatment of these diseases of the deeper structures.

This situation reminds one of the story of the haughty father who when a young man was seeking his daughter's hand in marriage, asked him with lofty superiority whether he could support her in the luxury to which she was accustomed, to which the young man replied, with a little irritation, for which I confess I think some justification may be found, that he ought to be able to because he had got her accustomed to it.

Or a surgeon arises who goes about preaching that all patients with cancer of the skin should come to him, for he is the person who knows how to cut out a cancer and he continues happily in his career of cutting out lupus chancres and gummas with the complacent idea that he is eradicating malignant growths at their beginning and so like the boy scout is doing his daily bit in the campaign for the control of cancer. He depends for his diagnosis on the laboratorian, both of them forgetting for the time how uncertain histologic diagnosis is without full clinical knowledge. Conservative pathologists realize the pitfalls in differentiating between epithelioma and other sorts of chronic ulcers of the skin and likewise in differentiating sarcoma from other chronic hyperplastic lesions of connective tissue, and all dermatologists can tes

tify to the mistakes that are made in diagnosing these conditions. Indeed, I have often felt that it would be a safe rule for a surgeon to have a dermatologist pass judgment on all lesions in the skin before operation. If the surgeons think, as I have no doubt they do, that the rule should work both ways, I am willing to have a surgeon pass judgment on the treatment of the same sort of lesions by a dermatologist before this is undertaken. I am vain enough to believe that the dermatologists would be more useful to the surgeons than the surgeons would be to the dermatologists. But I am willing to accept the advantages that the dermatologists would gain through the satisfaction, perhaps not altogether altruistic, of teaching them something about the skin. I hesitate at my temerity in offering this criticism of the surgeons, for I have an impression that they are touchy about their prerogatives, and I am likely to invite a counter-blast. I would not minimize their great capacity for usefulness. I am simply pointing out that even the surgeons are not at their best in some borderline fields. One could choose, I think, no better illustration of the dangers of spreading out one's field too thinly.

And now the psychoanalysts would treat diseases of the skin by laying open with the most painstaking dissections those primitive biologic urges that we dermatologists, who are still tainted by Victorian modesty, approach with reluctance because we are so unsophisticated as to feel that there are at least a few details of personal life that the individual might conceivably rather keep to himself and, indeed, might often be better off for not having emphasized in his attention before he has become a middle-aged crustacean. The psychoanalysts have one advantage. It takes so long for them to study a case that in the period of years that they require for examination the cutaneous disorders have the opportunity to demonstrate the fortunate tendency that they often show to get well of themselves.

We also have on us the endocrinologists and the physical therapists, with all their machinery, and the laboratorian, who is a bacteriologist in his first phase and an immunologist in his terminal phase, who apply their particular methods in any cases that they happen to bag in the terra incognita of dermatology.

Oh, this thing that is called life is a vexatious, trying experience to the dermatologists!

There is one consolation about it all. We are used to it, and with patience one can get used to almost anything. All physicians have to get used to it more or less. There is nothing new in the situation. Dear old Bishop Berkeley had a panacea in his tar water. Then Perkins with his tractors, mesmerism and hypnotism, galvanism, homeopathy and an unending list of treatments based on theories of disease have

filed past This state of affairs has been, after superstition, perhaps, the greatest stumbling block to medical progress As Huxley said, "Science commits suicide when it adopts a creed" Old Bonomo answered all of them when he commented, apropos of his discovery of the itch mite "From this discovery [that the itch mite causes scabies] it may be no difficult matter to give a more rational account of the itch than authors have hitherto delivered us It being very probable that this contagious disease owes its origin neither to the Melancholy Humour of Galen nor the corrosive acid of Sylvius, nor the particular ferment of van Helmont, nor the irritating salts in the serum or lymph of the moderns, but is no other than the continued biting of these animalcules in the skin"

It is a sad fact, but true, that the itch is still treated on the assumption that it is due to "the Melancholy Humour of Galen" It is a melancholy humor all right And that is where the poacher gets into trouble It does not do any good for the amateur or the professional psychoanalyst to bring out, after laying open his secret, that the young man's heart is bowed down by fear because of his one fateful indiscretion The laborious discovery of his secret will do no good, and it misleads the psychoanalyst One cannot reason with the itch, one cannot cast it out from a mind diseased, and one cannot even cure it with arsphenamine, under the impression, gathered from the history that the patient really has syphilis

That is the difficulty about cutaneous diseases One has to know what they are Dermatologists have to bear a great deal of joking about their elaborate and complicated nosology and nomenclature If our ridiculers knew how to diagnose a few cutaneous diseases it would not seem so amusing to identify them and have names for them The ludicrous thing is that scientific men do not realize that differential diagnosis is as necessary for diseases of the skin as for diseases of the kidneys or liver, for example

The inexorable necessity for making diagnoses is the difficulty that undoes all the groups who would treat cutaneous diseases (or any other diseases) by method rather than on the basis of diagnosis This necessity for making diagnoses is the difficulty—and the salvation—of dermatology Treatment by method does not work, and so one sort of enthusiasts follows another But the work of dermatologists, barring treatment of a certain fairly fixed percentage of mystical patients who must have something different, preferably something exotic, continues in the hands of those who know the itch when they see it, can tell lupus erythematosus from rouge do not treat impetigo with serum and do not treat lupus vulgaris gumma and epithelioma all in the same way

Treating by method rather than on the basis of diagnosis does not work well anywhere in medicine. The endeavor of medicine and all science for the last hundred and fifty years at least has been to secure factual knowledge, in contrast to hypothetical knowledge—to differentiate typhoid from typhus, chickenpox from smallpox and appendicitis from inflammation of the bowels before it is too late and to recognize that an organism and not some form of stroma is the essential cause of tuberculosis and that boils are due to pus organisms and not to "bad blood." It is this sort of scientific effort that brings about progress in medicine. If dermatology, because of the accessibility of its field, has gone further than most other specialties in differentiating pathologic processes, it is a scientific feat and a credit. And too, this has made dermatology a great deal more useful. It is not our fault that the finer detailed knowledge in the field is highly technical and requires an elaborate nomenclature—that is equally true of chemistry or botany, for example. There is only one thing that must be done by those who wish to cultivate the subject—that is to learn it. Of course, no group has any right to claim a natural monopoly of any field. The only claim that we can have on dermatology must be that we have better knowledge of it than others. If we cannot keep that position we do not deserve to control it and in time we will not.

But diseases of the skin are our field, it is regrettable that dermatology is so difficult to learn, but its very difficulty keeps the one-methodists from taking much of it for long.

In addition to the clinical complexity of dermatology, another fact marks it as a definite field. That is the fact that so large a proportion of cutaneous diseases not only are confined to the skin but are of local origin or are not involved in any disturbance of the general health, so far as can be determined, and one must know dermatology to recognize these. I am not saying, and I do not believe, that there are not many diseases of the skin that are produced or influenced by internal factors, but I am ready to maintain that physicians, including dermatologists, are inclined to overemphasize the importance of internal causes, that the more that is learned of diseases of suspected internal origin the more important local causes appear to be and that the internal treatment of cutaneous disease of unknown origin usually gets one nowhere.

Engman has given a fine phrase, "the skin, the mirror of the body." He had in mind that the skin shows practically all the pathologic processes that occur in the body and that in the skin they are exposed to direct view. From another standpoint one might with equal truth speak of the skin as the mask of the body. In a small group of systemic diseases the skin characteristically reveals internal disease, in a few others it does so in rare cases, but as a rule, far from being a gossip

about what goes on inside, it is a discreet protector of the body's secrets. Think of the vast multitude of conditions in which the skin is faithful to its function as a cover, concealing the distempers within nephritis, diabetes, cardiac and vascular disorders, tuberculosis, dyspepsia, carcinoma and even syphilis and nervous and mental diseases. It is not pleasant to think what a leprous-looking lot human beings would be if the skin really reflected the conditions inside the body. There is no more difficult part of dermatology than the interpretation of the general health from the condition of the skin and the interpretation of the condition of the skin from the general health.

And that is another reason that usually renders useless the treatment of undiagnosed cutaneous disease by the employment of measures which are empirically directed to defects in the general health which are surmised to exist or which, if existent, are actually irrelevant to the cutaneous disorder which the patient may have. One can make the "high liver" and the plethoric person unhappy by treating them for their gout or gouty diathesis as the cause of their cutaneous disorders, one can cut off their liquor and put them on buttermilk, and still their psoriasis, pruritus, ringworm or eczema goes on. One can feed iron to pasty-looking girls (who may or may not have anemia) until the iron market is affected. One can give constipated or listless patients yeast until one opens up unexpectedly a great outlet for that formerly modest and, in its place, useful commodity (as I believe has actually been done), and their acne, muddy complexion or eczema persists. This method of treatment does not work. One has to know the diseases that one is treating in the practice of dermatology. That is why dermatologists were born. And that, I doubt not, is why they will continue to exist for some time.

Is there any reason for joy to dermatologists in that thought? Even if we have a field of usefulness, is it a worth-while field, does it give its devotees in a reasonable degree the three sorts of reward—material, emotional and intellectual—that men have a right to expect in intellectual vocations?

I have had occasion recently to summarize this topic in another address, and I shall briefly refer to a few points here. The skin offers the great advantage that in it normal and pathologic tissues and functions are open to observation in their natural relation. Fortunately, also, as Auspitz long ago pointed out, "The skin's pathological features correspond entirely to the diseases of organs in general." It is in this sense that the skin is a mirror of the body. This fact has long been appreciated in medicine and has been specifically pointed out innumerable times.

The importance of the skin in general medicine is shown in many important illustrations. The present concepts of contagion, immunity and allergy had their beginning in the study of manifestations in the skin. Modern bacteriology and the modern methods of staining used in bacteriology and histology were first applied in studies of the skin. Manifestations of the effects of vitamins on the skin have been important in the development of the present knowledge of these substances. The one definite cause of cancer that is known, besides heredity, has been demonstrated in the studies of irritation of the skin. These are only a few of the many illustrations of the great fruitfulness of the study of the skin.

Dermatology has a field. It has its borderlines, which are not at all points distinct and may merge into other fields. Along these there are likely to be friction, as this also occurs on the ill defined borders between nations. But its great area is well defined, and we possess it not by right of possession but by right of discovery and useful occupation. As long as we hold it by that right it will remain ours. We need have no particular anxiety about the inroads of the highlanders who come down and raid our borders. "The good old rule, the simple plan, that he shall take who has the power and he shall keep who can" is sound ethics when it is applied to the rights of knowledge. As long as dermatologists justify the possession of their field by superior usefulness and scientific achievement they can hold it. And no one would wish that they hold it longer.

## BEJEL NONVENEREAL SYPHILIS

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DFIR-FZ-ZOR, SYRIA

Various aspects of *bejel*, the form of syphilis found among the Arabs of the valley of the middle Euphrates River, have been dealt with in previous papers from the clinic of the American Mission at Deir-ez-Zor.<sup>1</sup> Its nonvenereal aspect, however, has not hitherto received specific consideration, although *bejel* would seem to differ radically from conventional syphilis in this respect.

Sexual intercourse is so definitely linked with syphilis in clinical experience and scientific thought that the history of exposure to venereal disease through intercourse and the presence of genital primary lesions are recommended in textbooks to differentiate syphilis from other diseases. Syphilis without a venereal factor, though its possibility has been generally assumed and though some observers have even found it in isolated cases, has never been studied in a large population group and has remained largely hypothetical. My statement therefore, that syphilis does exist, as *bejel*, in a purely nonvenereal form in a Bedoun population numbering 150,000, demands proof.

In this paper I have presented my grounds for the belief that syphilis in the form of *bejel* is nonvenereal. The evidence lies along four lines: 1. The Bedoun villagers are prevented from sexual promiscuity by geographic, economic and social barriers. 2. The Bedouns, large numbers of whom have been treated in the clinic, are free from venereal lesions and diseases, and such venereal lesions and diseases as have been noted have occurred in other social groups. 3. The Bedouns say that there is no promiscuity among them and attribute the widespread propagation of *bejel* in their communities to infection through innocent contact, usually in childhood. 4. Experience with the clinical course of *bejel* confirms the fact that it is a nonvenereal community disease of the Bedouns acquired during childhood.

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1 (a) Hudson, E. H. Treponematoses Among the Bedoun Arabs of the Syrian Desert, U. S. Nav. M. Bull. **26** 817, 1928. (b) Hudson, E. H., and Young, A. L. Medical and Surgical Practice on the Euphrates River, Am. J. Trop. Med. **11** 297, 1931. (c) Hudson, E. H. Syphilis in the Euphrates Arab. A Clinical and Serological Study, Am. J. Syph. & Neurol. **16** 447, 1932, **17** 10, 1933. (d) Hudson, E. H., and Young, A. I. Arab Syphilis. Further Serological Studies. J. Christian M. A. India **8** 284, 1933. (e) Hudson, E. H. Joint-Articular Nodules in Euphrates Arabs, Tr. Roy. Soc. Trop. Med. & Hyg. **28** 511 1935.

## GEOGRAPHIC AND SOCIAL LIMITATIONS

A glance at any map of the Near East will remind one of the fertile crescent, beginning on the left with the Lebanon Mountains, running in a northeasterly curve along the south of Turkey and ending to the east in Irak. This well watered crescent enfolds a semiarid steppe known as the Syrian Desert, across which, radially to the arc, run the Middle Euphrates River and its tributary, the Khabur River. The town of Deir-ez-Zor lies near the junction of the rivers at a point about the middle of the chord subtending the crescent. The straight line length of the Euphrates River from the Turkish to the Irak border is about 250 miles (320 kilometers), and the length of the Khabur River is about 125 miles (160 kilometers).

The people who live along these two rivers are insulated from contacts with the outside world to a remarkable degree by the desert barrier, the nearest city being over 200 miles away, and most of the people still live as they have lived for milleniums. The settled population of the region numbers about 200,000, of which 195,000 are indigenous moslem Arabs<sup>2</sup>. This number does not include the nomad Arabs of the Syrian Desert, whose position and numbers fluctuate with the seasons and who are not included in the scope of this paper.

The Christian population of the region, numbering about 5,000, has little social significance and is not indigenous. The Christians are refugees and others whose homes are elsewhere, they are to be found only in the towns.

The indigenous Moslems who comprise the bulk of the population are divided into two distinct social groups, in one group I have placed the townsmen and in the other, the Bedouins. The townsmen number 50,000, of whom 35,000 live in Deir-ez-Zor and the remainder in four small towns on the Euphrates River, namely, Rakk, Sabkha, Meyadin and AbuKemal. Of the Bedouins, 132,000 live in small mud villages along both banks of the Euphrates River, and 13,000 live similarly along the Khabur River.

Among the Christians, the patronage of prostitution exists to a degree closely comparable to that in the West. Syphilis among them is known as *fianghi* (the disease of the Frank, or westerner), and the name carries with it the connotation of venereal origin and of shame.

The name given to syphilis among the townsmen depends on its source in a given case. A townsman who has contracted syphilis through venereal contact refers to it as *fianghi*, whereas childhood infection among the townspeople is given the Bedouin name of *bcjel*. The infants of town families are often sent out to the Bedouin villages

<sup>2</sup> The figures on population which are given here are all approximate but are based on an accurate census now being made by the government in Deir-ez-Zor.



to spend the first year or two of life. They may thus contract *bejel*. In other instances *bejel* may appear among the children of a town family through some contact in a village. Thus, many of the adult townspeople have had infection with *bejel* in childhood, and I have seen some cases in which it seemed likely that there had been a nonvenereal infection in childhood with *bejel* and a venereal infection in adult life with *fianghi* in the same patient. In none of these cases, however, could the observations be checked scientifically.

In general, *bejel* is dying out in the towns. My associates and I see much less *bejel* in town children than we did ten years ago. Most persons in the town now receive some treatment.

The Bedouins call their type of syphilis *bejel*, it has the connotation of a childhood exanthem, and the Bedouins say they have had it without shame. They recognize that the children of their communities are the great reservoir of the acute form of the disease and that adults who have escaped the infection in childhood usually contract it from children, often their own, later in life. They state that there is no sexual promiscuity among them, and they resent any suggestion that *bejel* is the same as *fianghi*, because the latter term has a venereal connotation.

Though most of the town families sprang originally from Bedouin stock, townsmen and Bedouins are now sharply demarcated by social distinctions of dress, language and mode of life. Especially are they to be distinguished in their economic status.

The townsmen comprise shopkeepers, money-lenders, landowners, middlemen, pedlers, artisans, officials and professional men of religion and law. The Bedouins in their villages along the two rivers combine cereal farming with sheep raising. They are virtually seminomads. They wage an unequal and continual struggle against floods, locusts, drought and extremes of heat and cold. The economic status of the townspeople is comparatively high, while that of the Bedouin is just above the level of starvation.

The Bedouins never live in town, seldom stay in town overnight and mingle with the townspeople only as they chaffer and bargain in the bazaars. They reach the town on donkeys or on foot, following the path along the river, and the towns of the region are so few that such journeys often consume two or three days. The villager supplies most of his own scanty needs and seldom leaves his home to dispose of his farm products. His money-lender and landowner are on hand at the harvest to take their share and bargain for the surplus. There are no fairs for trade and jollification, such as are often found among the peasantry in other countries. Few of the young Bedouin men enter the army, and none of the Bedouin children attend the town schools.

The townspeople despise the Bedouins as dirty and uncouth, the dislike is mutual, and one group can hardly refer to the other without

a curse. The Bedouin is the butt of the jokes and ill humor of the market place and is pushed off to one side in the cafés. Feeling himself at a disadvantage in the bonds of city walls and conventions, he is always glad to return to the open spaces of the river and the desert. He has not time, money or opportunity to patronize the houses of prostitution, the cinemas or the dancing entertainments of the town. Finally, he does not touch alcohol in any form. There are brothels in the towns and also much clandestine prostitution, but the women cater only to townsmen and soldiers. Bedouins are not solicited, and a Bedouin would be thrown out and probably beaten by the other patrons if he tried to enter a brothel.

Thus, the Bedouin men, owing to their own poverty and to social barriers raised against them, have practically no venereal contacts in the towns. Then how much prostitution and promiscuity is there in their own villages? Here a very severe social code operates to reduce promiscuity to a negligible quantity. The Arab, though primitive in many respects, has a highly developed sense of sexual propriety, which the closely knit clan life of the community still preserves. The Arab law on matters of sex is based on the value of the child-bearing woman as the mother of sons, who are the fighting power of the tribe. If a Bedouin man is sexually impotent his wife's family have the right to declare the marriage void and select another husband who can "raise up sons."

The wealth of a Bedouin is measured in daughters as well as in sons, in fact, from the standpoint of money, daughters are assets and sons are liabilities. In each village and tribe the value of a marriageable daughter is fixed by custom. In the region of Deir-ez-Zor the market price of a girl is from fifteen to twenty sheep, 30 bushels of wheat and a camel or 3 Turkish gold pounds. The total value would represent perhaps 22 gold pounds, or about \$150. At current wages, a Bedouin working for Bedouins would require from one to two years to earn this amount in daily labor. Some of the sheiks hold their daughters for prices up to 200 gold pounds.

Though many fathers pay the marriage price for their sons' brides and many other marriages are arranged by exchange, there remain many young men who have to work years before they can afford the purchase price of a wife. Under these circumstances it is obvious that the father of daughters has a strong commercial motive reinforcing his natural repugnance to antemarital promiscuity on the part of his daughters, and he consequently guards them well.

The penalty for rape is very severe. Rape by night is punished less severely than rape by day, because in view of the distribution of the day's labor the woman is more likely to be alone during the day whereas

at night she is supposed to be under the care of her male relatives. An unmarried woman who becomes pregnant is likely to be killed by her brothers as a matter of family honor, and if she identifies the father of the child her brothers may kill him also or exact a heavy fine. Arab law does not recognize any "age of consent" on the part of the woman. No matter how mature she may be, power of consent to her marriage is always lodged in her father or, if he is dead, in her oldest brother.

When one sees the intimate way in which the villagers live and the simplicity of their family and community life, it is difficult to imagine the possibility of much clandestine sexual promiscuity. Girls are usually married as soon as child-bearing becomes possible, large families are the rule, the woman is a responsible and important member of the family and the tribal organization, and husband and wife usually hold positions of mutual esteem. When the first wife has aged with hard work and child-bearing the man may marry another and younger woman, but this is done naturally, without derogation to the status of the first wife. The tribal organization does not tolerate an unmarried woman, and one is very rare.

To sum up these observations. Prostitution is found only in the towns, the brothel is easy of access only to townsmen. The Bedouin is not a welcome guest in the town, he lives at a great distance, he works hard the entire year, he has little money and little interest in the amusements in town, he seldom enters military service, and he does not touch alcohol. In their own close-knit communities the Bedouins do not tolerate sexual promiscuity, rape is severely punished, marriage is made by purchase, with a high cash premium on virginity, and girls are always married at an early age.

On these a priori grounds, venereal disease should be rare among the Bedouins. This conclusion is supported by clinical data.

#### CLINICAL DATA

The consideration of the clinical material is divided into three parts. On the assumption that venereal disease in a given community is most likely to be found in its overt aspects among the men, I shall first discuss the syphilitic history and lesions of all the males 15 years and older admitted to the clinic in the course of 5,000 consecutive general new admissions. One may also assume that the incidence of gonorrhea in a community is a valuable check on the existence of promiscuous sexual intercourse. Therefore, in the second part of this section I shall analyze all the cases of gonorrhea in males and females observed in the clinic in the course of 7,000 consecutive general new admissions. In the third part of this section I shall indicate what I believe is the answer to the question: How then if it is not venereal, is *bejel* propagated?

1 *Syphilitic Males*—Proportion of Social Groups Among Patients During the three years ending June 30, 1934, 4,355 different men, women and children were admitted to the clinic in Deir-er-Zor. Of these, 970 (22.3 per cent) were former patients, and 3,385 (77.7 per cent) were newly admitted. Of the 3,385 new patients, 799 (23.6 per cent) were Christians, 1,202 (35.5 per cent) were townspeople and 1,384 (40.9 per cent) were Bedouins.

Proportion of the Sexes Among New Patients. Previous statistical studies have shown<sup>3</sup> that the new patients in the clinic were divided approximately equally between the sexes.

Proportion of Syphilitic and Nonsyphilitic Males Among 2,500 New Patients. Between June 27, 1932, and Sept. 1, 1934, 2,500 new patients were admitted to the clinic. During this period there were admitted 870 males of 15 years and older, of whom 518 (59.5 per cent) were not syphilitic and 352 (40.5 per cent) were syphilitic.

Of these 870 males, 179 were Christians, of whom 21 (11.7 per cent) were syphilitic and 158 (88.3 per cent) were not syphilitic. There were 274 townsmen, of whom 57 (20.8 per cent) were syphilitic and 217 (79.2 per cent) were not syphilitic. There were 417 Bedouins, of whom 274 (65.7 per cent) were syphilitic and 143 (34.3 per cent) were not syphilitic.

Thus, in a consecutive series of 870 men admitted to the clinic, two-tenths were Christians, with an 11.7 per cent incidence of syphilis, three-tenths were townsmen, with 20.8 per cent incidence of syphilis, and one-half were Bedouins, with a 65.7 per cent incidence of syphilis.

Observations on 660 Syphilitic Men. Between Jan. 27, 1930, and Sept. 1, 1934 (three years and seven months), exactly 5,000 new patients were admitted to the clinic. Of these, approximately 2,500 were males. The exact number of men 15 years and older was 1,763.

Of these 1,763 men 15 years and older, 660 (37.4 per cent) were syphilitic according to diagnosis and 1,103 (62.6 per cent) were not syphilitic. Of the 660 syphilitic men, 50 (7.6 per cent) were Christians, 156 (23.6 per cent) were townsmen, and 454 (68.8 per cent) were Bedouins.

Thus, though 23.6 per cent of the new patients were Christians, only 7.6 per cent of the syphilitic males were Christians. Though 35.5 per cent of the new patients were townspeople, only 23.6 per cent of the syphilitic males were townsmen. On the other hand, the Bedouins comprised 40.9 per cent of those newly admitted but furnished 68.8 per cent of the syphilitic males.

Ages of 660 Syphilitic Men. Of the 660 syphilitic men 15 years and older, 39 were between 15 and 19 years, 222, between 20 and 29 years, 203, between 30 and 39 years, 97, between 40 and 49 years, 46, between 50 and 59 years, 40, between 60 and 69 years, and 13, 70 years or older. Thus, 261 (40 per cent) were between 15 and 29 years of age, and 464 (70 per cent) were below the age of 40 years. In other words, 70 per cent of this series of syphilitic men were within the age when venereal disease is most common. One hundred and ninety-six (30 per cent) were over 40 years of age.

Anamnesis of 50 Syphilitic Christians. Of the 50 syphilitic Christian men, 1 had contracted *bejel* from the Arabs when a refugee in childhood. Eighteen gave a definite age of infection with *fianglu* as follows: 3 between 15 and 19 years, 12 between 20 and 29 and 3 between 30 and 39 years. Six did not state the age of infection, 4 were uncertain, and 21 said they did not have an infection.

3 Hudson<sup>1b, c</sup> Hudson and Young<sup>1a</sup>

Of the 6 who did not state the age of infection, the Kahn reaction of the blood was doubtful for 1 and positive for 5. Of the 4 who were uncertain about infection, the Kahn reaction of the blood was negative for 1 and positive for 3. Of the 21 who said they did not have syphilitic infection, the Kahn test of the blood was not carried out on 2, and the reaction was negative for 3 and positive for 16.

**Anamnesis of 156 Syphilitic Townsmen** Of the 156 syphilitic townsmen, 55 (35 per cent) said they had had *bejel* in childhood. Twenty-eight gave a definite age of later syphilitic infection as follows: 5 between 15 and 19 years, 14 between 20 and 29 years, 5 between 30 and 39 years, 2 between 40 and 49 years, and 2 between 50 and 59 years. Twenty-two did not state the age of infection, 9 were uncertain and 42 said they did not have an infection.

Of the 22 who did not state the age of infection, the Kahn test was not carried out on 3, and the reaction was doubtful for 1 and positive for 18. Of the 9 who were uncertain about infection, the Kahn reaction of the blood was negative for 3 and positive for 6. Of the 42 who denied syphilitic infection, the Kahn test was not carried out on 3, and the reaction was negative for 8 and positive for 31.

**Anamnesis of 454 Syphilitic Bedouins** Of the 454 seminomadic syphilitic men, 287 (63 per cent) said they had had *bejel* in childhood. One hundred and nine (24 per cent) gave a later age of infection as follows: 15 between 15 and 19 years, 50 between 20 and 29 years, 33 between 30 and 39 years, 7 between 40 and 49 years, 2 between 50 and 59 years and 2 between 60 and 69 years. Ten did not state the age of infection, 20 were uncertain and 28 said they did not have infection.

Of the 10 who did not state the age of infection, the Kahn reaction of the blood was negative for 1, doubtful for 1 and positive for 8. Of the 20 who were uncertain about infection, the Kahn test was not carried out on 3, and the reaction was negative for 5, doubtful for 1 and positive for 11. Of the 28 who said they did not have infection, the Kahn test was not carried out on 4, and the reaction was negative for 6 and positive for 18. One of the patients with a negative Kahn reaction of the blood had a positive reaction of the cerebrospinal fluid.

Thus, of 50 syphilitic Christian men, 25 (50 per cent) gave a history of infection, of 156 syphilitic townsmen, 105 (67 per cent) gave a history of infection, and of 454 syphilitic Bedouins, 406 (90 per cent) gave a history of infection. In other words, only half the Christians admitted having syphilitic infection, while two thirds of the townsmen and nine tenths of the Bedouins did so.

**Reactions of the Blood of 660 Syphilitic Men** <sup>4</sup> Of the 50 syphilitic Christians there was a record of Kahn reactions of the blood for 47. Of this number, 9 had a negative reaction (all doubtful reactions are counted as negative), but 1 with a negative reaction of the blood had a positive reaction of the spinal fluid. This makes a corrected total of 8 (17 per cent) with a negative and 39 (83 per cent) with a positive reaction. The positive reactions were distributed as follows: 9, 1+, 16, 2+, 6, 3+, 7, 4+, and 1 (cerebrospinal fluid), 1+.

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<sup>4</sup> All the serologic work hitherto done, as well as that reported on here, has been carried out according to the Kahn method in the laboratory of the clinic. Through the courtesy of Bedouins of the American University of Beirut Medical School, a series of specimens of serum is also being tested in the laboratory of the American Hospital in Beirut by both the Kahn and the Kolmer-Wassermann methods. The results in the two laboratories and with the two types of reaction show close parallelism and will be reported on subsequently in full.

Of the 156 syphilitic townsmen, there was a record of the Kahn reaction of the blood for 143. Of this number, 27 (19 per cent) had a negative reaction, and 116 (81 per cent), a positive reaction. The positive reactions were distributed as follows: 48, 1+, 41, 2+, 20, 3+, and 7, 4+.

Of the 454 syphilitic Bedouins, there was a record of the Kahn reaction of the blood for 384. Of this number, 67 had a negative reaction, but 2 of these had a positive reaction of the spinal fluid. This makes a corrected total of 65 (17 per cent) with a negative and 319 (83 per cent) with a positive reaction. The positive reactions were distributed as follows: 98, 1+, 107, 2+, 63, 3+, 49, 4+, 1 (cerebrospinal fluid), 1+, and 1 (cerebrospinal fluid), 2+.

Thus, the Kahn test was carried out on 574 of the 660 syphilitic men. Approximately 83 per cent of the whole series and 83 per cent of each of the constituent groups had a positive reaction. This is a comparatively high percentage of positive reactions, as two factors are neglected, both of which have a tendency to

TABLE 1—*Syphilitic Lesions and History of Exposure to Venereal Infection in 660 Syphilitic Men*

	50 Christians (franghi)	156 Townsmen (franghi or bejel)	454 Bedouins (bejel)
<b>Syphilitic lesions</b>			
Ulcers of mouth, nose and throat	3	28	175
Ulcers and eruption of skin	4	18	162
Periostitis	1	4	45
Arthritis and effusions into the joints	0	3	15
Juxta articular nodules	0	1	7
Plantar keratosis	0	0	7
Exostoses	0	0	2
Orchitis	2	5	8
Penile ulcers	0	1	6
Chancres	21	15	0
Buboes	3	3	1
Tabs dorsalis	1	2	0
Hemiplegia	0	1	0
<b>History</b>			
Habitual venereal exposure	12	12	0
Acute or chronic gonorrhea	10	10	0

reduce the percentage of positive reactions. First, some of the patients, especially those of the Christian group, had had treatment for syphilis before the blood was tested. Second, many of the patients, especially those of the Bedouin group, had a latent infection dating back decades to a childhood infection.

**Syphilitic Lesions and Venereal History of 660 Males.** In table 1 are indicated the types of lesions found in 660 syphilitic males and also significant facts relating to exposure to venereal disease. The table is divided into three parts, showing the lesions in Christians, townsmen and Bedouins. It will be noted that ulcers of the mouth, nose, throat and skin and lesions of the periosteum were much more common among Bedouins and that chancres, gonorrhea and a history of exposure were confined to the Christians and townsmen.

It will be noted that of the 660 syphilitic males there were only 36 with initial lesions, i. e., chancres, and that these appeared in 21 of the 50 Christians and in 15 of the 156 townsmen. None of the 454 Bedouins presented a chancre. The penile ulcers found in 6 Bedouins were late lesions. In an experience of ten years I have never seen a chancre on a Bedouin subject, using the word in the usually accepted sense of a genital initial lesion.

**Summary** To sum up this section, 40 per cent of the men admitted to the clinic were syphilitic 12 per cent of the adult male Christians, 21 per cent of the adult townsmen and 66 per cent of the adult male Bedouins In a series of syphilitic males, 75 per cent were Christians, 23.5 per cent were townsmen and 69 per cent were Bedouins In the same series, infection with syphilis was acknowledged by only half of the Christians, by two thirds of the townsmen and by nine tenths of the Bedouins The Christians contracted the disease venereally, the townsmen, either venereally or nonvenereally, and the Bedouins nonvenereally Two thirds of the Bedouins acquired syphilis in childhood A history of repeated venereal exposure and of gonorrhea was obtained only from Christians and townsmen Genital chancres were found only on Christians and townsmen Syphilitic lesions of Bedouin men were mostly late manifestations of the disease, in the mouth, nose and throat, on the skin and in the bones and joints

**2 Gonorrhea Among 7,000 New Patients**—One might disregard the foregoing sociologic and clinical facts, which support the Bedouins' own statement that sexual promiscuity does not enter into the propagation of *bejel*, and—taking their own admission that most of them contract *bejel* in childhood—one might argue that the absence of chancres in Bedouin men was due merely to the early and thorough dissemination of the syphilitic virus among the men and women throughout the community The absence of chancres under such conditions would not rule out the possibility of sexual promiscuity

A control which helps to settle this point is found in gonorrhea, an independent venereal disease that elsewhere runs parallel to the distribution of venereal syphilis Crucial evidence that sexual promiscuity does not exist among the Bedouins is furnished by the statistics on gonorrhea, a disease which is probably an even clearer index of promiscuity than syphilis

The records of 7,000 consecutive new patients admitted to the clinic showed 149 cases of gonorrhea, with 98 in men and 51 in women In 72 of these cases smears were positive for the gonococcus, in the rest the smears were negative or there was no bacteriologic examination, the diagnosis being based on clinical symptoms and a history of exposure to venereal disease

Of the 98 males, 55 were Christians, 41 were townsmen and 2 were nomad Bedouins, for 1 of whom the diagnosis was doubtful (the other had been a soldier and admitted frequent exposure to venereal disease through intercourse) Of the 51 women, 30 were Christians and 21 were townswomen

The records of the clinic do not show any Bedouin woman with gonorrhea or with any of the sequelae of gonorrhea Dr Susan Croslev<sup>5</sup> stated that in five years of gynecological work in the clinic, during which she examined hundreds of Bedouin women, she had not seen an instance of gonorrheal cervicitis, pelvic inflammation or any of the other conditions associated with this disease in women

5 Personal communication to the author

Ninety-six of the 98 men with gonorrhea were Christians and townsmen. Two were nomads of the eastern desert, of whom 1 was a soldier and might well be reckoned with the townsmen. The series did not contain any Bedouin villagers. In my experience of examining perhaps 2,000 Bedouin men I have never seen one with gonorrheal urethritis, gonorrheal orchitis, epididymitis, stricture or other manifestation of gonorrheal infection in the male. The clinical examination of these men and women has been too thorough to permit the assumption that gonorrheal infection, if present, would be overlooked even though not included in the patient's complaints.

The conclusion is inescapable that the Bedouin community is free from gonorrheal infection, a fact that strongly supports the assumption that the Bedouins do not indulge in sexual promiscuity.

3 *Bejel*, a Childhood Disease of the Whole Community—Up to this point I have been presenting the evidence that promiscuity and

TABLE 2—*Bedouins' Statements as to Time of Infection with Bejel (1,000 Cases)*

Time of Infection, Years	Men	Women	Children	Total
0 to 14	219	236	103	558
15 to 19	18	17	0	35
20 to 29	25	33	0	58
30 to 39	12	13	0	25
40 to 49	7	5	0	12
50 to 59	4	0	0	4
60 to 69	3	2	0	5
Never	13	23	4	40
Never, but . . . . .	39	68	89	216
Kahn reaction negative	70	33	25	88
Kahn reaction positive	16	11	9	36
No test	10	24	55	92
Total	360	397	196	953
Blank records				47
Total				1,000

venereal diseases do not exist among the Bedouin villagers and therefore that syphilis (*bejel*) as it exists among them is not venereal. The negative statement is not sufficient, however, and I shall indicate in this concluding section what seems to be the true nature and course of *bejel*.

*Time of Life When Bejel Is Contracted* In a case of venereal syphilis the element of shame clouds the patient's anamnesis, the Bedouins, on the contrary, readily acknowledge previous infection with *bejel*, and their statements have a high degree of accuracy, as shown by a check with their reactions to the Kahn test.<sup>6</sup>

In the first series of 177 syphilitic Bedouins,<sup>10</sup> 80 (45 per cent) said they had had *bejel* in childhood and 46 (26 per cent) named a later specific date of infection.

In a series of 162 apparently healthy Bedouin workmen,<sup>11</sup> 91 (56 per cent) said they had had *bejel* in childhood and 41 (25 per cent) named a later specific date of infection.

In a series of 62 Bedouin patients<sup>12</sup> examined at a distance of 60 miles (82.2 kilometers) from Der-ez-Zor, 29 (45 per cent) said they had had *bejel* in childhood and 19 (30 per cent) named a later specific date.

<sup>6</sup> Hudson<sup>10</sup> Hudson and Young<sup>11</sup>



In the anamnesis of the 454 syphilitic Bedouin men mentioned in an earlier part of this paper 287 (63 per cent) said they had had *bejel* in childhood and 109 (24 per cent) named a later specific date of infection

The largest series of such statements is summarized in table 2. Between April 4, 1933, and March 27, 1935, 2,307 patients of all kinds were admitted to the clinic, of whom exactly 1,000 were Bedouins of all ages. Of these 1,000 Bedouins the patient's statement in regard to infection with *bejel* is lacking for 47. Of those whose statements were recorded, 360 were men, 397, women, and 196, boys and girls aged from new-born infants to 14 years.

Of the 360 men, 219 (61 per cent) said they had had *bejel* in childhood, and 69 (19 per cent) named a later specific date. Only 26 had the first infection with *bejel* after the age of 30, and 13 were uncertain. Fifty-nine stated they did not have syphilitic infection, 16 of these had a positive Kahn reaction.

Of the 397 women, 236 (59 per cent) said they had had *bejel* in childhood, and 70 (18 per cent) named a later specific date. Only 20 had the first infection with *bejel* after the age of 30. Twenty-three were uncertain. Sixty-eight stated they did not have syphilitic infection, 11 of these had a positive Kahn reaction.

Of the 196 children, 103 (52 per cent) were said to have had *bejel*, either in infancy or in earlier childhood, and 4 were uncertain. Eighty-nine stated they did not have syphilitic infection, 9 of these had a positive Kahn reaction.

For the whole series of 1,000, including patients whose statements were lacking and children who had not yet had *bejel*, 55.8 per cent had had *bejel* in childhood and 13.9 per cent named a later specific date of infection, 4 per cent were uncertain and 21.6 per cent stated they did not have infection.

There were 757 patients, male and female, 15 years and older, of whom 455 (60.1 per cent) had had *bejel* in childhood, 139 (18.4 per cent) others had had *bejel* at a later specific time, making a total of 594 (78.5 per cent) who acknowledged syphilitic infection. Only 46 (6 per cent) had had the initial infection after the age of 30.

The Kahn reactions for those who said they did not have infection supported the patients' statements in 2 cases of 3 among the men and in 3 cases of 4 among the women and children.

Thus, in a Bedouin population in which over 60 per cent had a positive Kahn reaction,<sup>1d</sup> 60 per cent of a large series said they had had *bejel* in childhood and another 20 per cent said they had had it at a later specified date, only 6 per cent said they contracted it after the age of 30.

This is evidence not only that *bejel* among the Bedouins is not a venereal disease but that it has a community-wide distribution and that it is usually acquired in childhood.

*Clinical Course and Apparent Epidemiology of Bejel*.—The Bedouin child is not congenitally syphilitic, though both parents have usually had *bejel*. It may be that the child carries over from birth a state of allergy to the syphilitic virus, which perhaps accounts for the par-

<sup>7</sup> This summary is based on experience with the disease in the clinic. The underlying clinical and laboratory findings are to be found in the papers already published and in preparation.

ticular way that he reacts to the disease when he contracts it. This point needs to be investigated by the use of the cutaneous test with organic luetin in children who have not yet had *bejel*.

At some time in early life the Bedouin child contracts *bejel*, the source of the infection being some other child in the acute stage of the disease. As this stage lasts several months and does not incapacitate the subject and as the children of the village play together, it is easy to see how few children escape contact with the disease.

In humid, tropical countries where vegetation is luxuriant, wounds and scratches are common and heal slowly, offering suitable sites for the implantation of infection by contact or through the medium of the multitude of insects. These climatological features account for the superficial position of initial spirochetal lesions in the tropics. In contrast, the region of Deir-ez-Zor is a dry steppe or desert, with an annual rainfall of about 5 inches (127 cm) and with little vegetation. Cutaneous wounds and abrasions are therefore rare and tend to heal promptly without suppuration when they do occur. This may account for the absence of initial lesions on the skin in *bejel*, the mother sore. Such lesions are never recognized or indicated by the patient with *bejel*.

On the other hand, the Bedouin method of supplying drinking water for the family offers ample opportunity for the transfer of spirochetes and probably determines the usual site of the earliest lesions of *bejel*. The women carry up from the river skins of water, which are laid in the darkened huts. A small bowl without a handle is used to drink from, and every one has recourse to this bowl many times a day. The domestic fly, the louse and the flea are the three ubiquitous insects of the Bedouin hut or tent, and they may also play some part as vectors of the virus. The legions of flies in particular may carry infection from lip to lip. The adults frequently fondle and kiss the children. Altogether, it is not surprising that oral lesions are usually the first to appear in *bejel*.

The child with *bejel* does not usually show much constitutional change, and the Bedouins say that children never die of *bejel*. The lesions on the mucous membrane of the oral cavity are grayish patches with desquamation but with no ulceration. The saliva and scrapings of the lesions swarm with spirochetes of the morphology and characteristic motility of *Spirochaeta pallida*<sup>8</sup>. About the same time the patches occur in the mouth papules appear about the genitalia and in the folds of the skin. Sexual intercourse does not determine this location.

<sup>8</sup> Dark-field studies of lesions of *bejel* are now in progress. The special objective and lamp for this purpose were provided by a grant made by the Ella Sachs Plotz Foundation, and the special condenser was the gift of friends in Collingswood, N. J.

Papules are most common and most succulent where there is warmth and moisture. Other papules may appear on the trunk, usually arranged in circinate configurations. Spirochetes are easily demonstrable on the moist papules. The process in the oral cavity may extend to the bones of the nose, producing softening and collapse of the nasal bridge. Less often, there are tenderness and swelling of the epiphyses and periosteum of the long bones.

In the course of a year these lesions disappear, leaving an apparently healthy child. Few of the Bedouin children are ever presented to a physician, as the Bedouins recognize the infection as inevitable and self-limiting. Few receive curative treatment, though an injection or two of an arsenical or of a bismuth preparation will abolish the lesions.

The child with *bejel* always has a strongly positive Kahn reaction of the blood, which remains positive for many years, though as he grows up he may present no further symptoms of the disease. At some time later, however, in the second, third, fourth, fifth, sixth or even seventh decade of life, there may develop an ulcer of the pharynx, an ulcer or eruptive patch on the skin or a gumma of the nasal bones or one of the long bones. Or the subject may merely complain of aching and throbbing in all the bones of the body.

When some of these late lesions break down one may find spirochetes, but there is usually an enormous admixture of secondarily infecting organisms. Again, 1 or 2 Gm of an arsenical or 1 Gm of a bismuth preparation will usually suffice to abolish the lesion. The interval between the first infection with *bejel* and the appearance of these late lesions is usually so great that the Bedouins have not learned to connect them as being due to the same cause.

There is absence of serious damage to the cardiovascular system, the nervous system or viscera.<sup>10</sup> The rate of miscarriage is much lower than that found in women with venereally contracted syphilis.<sup>9</sup>

If a man has escaped the infection in childhood and subsequently marries, he does not contract syphilis from his wife, though she probably had *bejel* in childhood. But he is almost sure to become infected at some time in his life by contact with some child, perhaps his own who has open lesions on the mouth. Many of the adult patients with *bejel* give this history spontaneously. When the adult contracts the disease the lesions on the mouth develop first, and then the lesions on the skin and other parts of the body, in the same sequence as *bejel* in the child. In the adult, however, the early lesions often have a tendency to pass directly into the late lesions without an interval of time.

9 These aspects of *bejel* will be considered separately in subsequent papers.

The previously reported studies<sup>6</sup> of the reaction to the Kahn test in the Bedouins showed the same percentage of positive reactions in men and in women of all age groups. The percentage is about 60, whether in patients in the clinic or in presumably healthy persons who are not patients.

The foregoing clinical résumé of *bejel* shows that it is a disease of the whole Bedouin community, resembling a childhood exanthem in its epidemic course.

#### COMMENT

In the valley of the Middle Euphrates River, within the territory of the Syrian mandate, is a region isolated from outside contacts, with a population of 200,000, comprised of 5,000 Christians, 45,000 Arab townsmen and 150,000 seminomad Bedouin villagers.

About 1,400 general new patients per year are admitted to the Den-  
ez-Zoi Clinic, of whom 24 per cent are Christians, 35 per cent towns-  
people and 41 per cent Bedouins. The three groups are distinct socially  
and differ in their relation to sexual promiscuity and venereal diseases.

Members of the general Christian population, with an incidence of syphilis of less than 10 per cent (mostly the young men), have venereal syphilis, called *fianghi*. Men and women of the Christian group have gonorrhea.

Members of the general Bedouin population, with an incidence of syphilis of over 75 per cent, suffer from nonvenereal syphilis called *bejel*, a disease of the whole community, affecting persons of all ages and both sexes. Neither Bedouin men nor Bedouin women have gonorrhea.

The general town population, with an incidence of syphilis of about 25 per cent, is an intermediate group, some having *fianghi*, if they have contracted syphilis venereally in adult life, and others having *bejel*, if they contracted the disease nonvenereally in childhood. Gonorrhea is found in both sexes among the townspeople.

In other words, in this small geographic area syphilis exists in two forms, (1) the purely venereal type and (2) the purely nonvenereal type. The definiteness of these two forms of syphilis in such close physical proximity is linked with and explained by peculiar economic and social factors and is probably not to be duplicated elsewhere.

If this region is opened by roads, commerce and contacts with the outside world, as may indeed happen, the distinctiveness of the three social groups is bound to fade and with it the distinctiveness of the two forms of syphilis.

The present freedom of the Bedouins from promiscuous habits and from venereal diseases is bound to be lost as their customs break down in contact with the forces of civilization. A rise in the economic level,

a more ready access to the towns, a growth of individualism and a loosening of the tribal bonds would all tend to the introduction of promiscuity and venereal diseases. These Bedouins are by no means paragons of sexual morality. Only the combination of isolation, straitened economic conditions and a rigid tribal sexual code maintains their present freedom from venereal diseases.

The process of disintegration is already apparent in their cousins, the townspeople, and the similar disintegration of the villagers will probably not long be delayed. Hewer<sup>10</sup> attributed the introduction among the Arabs of the Sudan of gonorrhea (which is now universal) and syphilis (which now exists "side by side with yaws") to the breaking down of local social barriers and the consequent dissemination of imported diseases.

The juxtaposition of *fianghi* and *bejel* in the region of Deir-ez-Zor brings into focus the fact that the character of syphilis varies with the particular epidemiology of its locale. *Bejel* operates under the epidemiologic triad of (1) widespread community infection, (2) childhood acquisition and (3) general lack of treatment. *Fianghi* occurs in a restricted adult portion of the towns and is definitely venereal. *Fianghi* and *bejel* have in common the etiologic agent, the reaction of the blood and the favorable response to the same drugs, but the clinical courses in the human subject are strikingly different.

That *bejel* is a spirochetosis is beyond doubt. The uniformly positive reactions of the blood and the constant presence of a spirochete with the morphology and motility of *S. pallida* in dark-field preparations from the early open lesions settle this point. It is possible that *bejel* is the manifestation of a peculiar strain of *S. pallida*. This point can be settled only by experimentation on animals.

The parallelism of *bejel* and yaws is impressive. Yaws operates under the same epidemiological triad as *bejel*. But to call *bejel* yaws would be to create more difficulties than would be solved. The clinical course of the two diseases, though remarkably similar, is not identical. Stannus said<sup>11</sup> "I should like to emphasize the fact that yaws is strictly a tropical disease limited by Cancer and Capricorn." Stitt<sup>12</sup> made the same statement and added that it is found almost exclusively in the dark-skinned races. Deir-ez-Zor is over 10 degrees north of the Tropic of Cancer, and the Bedouins are Semites, not related to the

10 Hewer, T. F. Some Observations on Yaws and Syphilis in the Southern Sudan, *Tr. Roy. Soc. Trop. Med. & Hyg.* 27: 593, 1934.

11 Stannus, H. S. Yaws and Syphilis, *Brit. J. Ven. Dis.* 4: 55, 1928.

12 Stitt, E. R. The Diagnostics and Treatment of Tropical Diseases, ed. 5, Philadelphia, P. Blakiston's Son & Co., 1929.

dark-skinned races. It would be hard to picture a pocket of yaws developing in this area so far from the regions in which yaws is endemic.

It would be gratuitous to introduce yaws as an explanation of the character of *bejel* or even to bring in the concept of a special strain of virus when a simpler explanation is at hand, one that meets the demands of the equation adequately. It seems to my associates and me that such an explanation does exist and that the true explanation may be stated as follows. The dissimilarity in the epidemiology of *bejel* and *fianghi* accounts for the difference between these forms of spirochetosis, and the similarity in the epidemiology of *bejel* and yaws accounts for the likeness of these two forms of spirochetosis.

It has been assumed in the literature that there is such a disease entity as acquired nonvenereal syphilis of childhood, such as *bejel*. Stannus said <sup>11</sup>

Infection with syphilis may, and does, take place in childhood in some native communities where the disease is widespread, and the primary lesion is then commonly extragenital. Many observers, writing of syphilis among native children, appear to believe they are dealing with the inherited disease, and note with surprise the absence of some of the common stigmata, whereas I believe they are dealing with late syphilis, the disease having been contracted in infancy, and it must never be lost sight of that tertiary lesions often appear early. For comparison with the pathology of yaws, I would suggest that a study of the pathology of syphilis in a native race be undertaken. There is a good deal of evidence that the manifestations of that disease among indigenous natives differ somewhat from those seen in Europeans, evidences that the reaction to infection tends to differ in the two cases.

In a previous paper <sup>12</sup> from the Deir-ez-Zor Clinic the following statement was made:

Most writers and reviewers of literature of tropical medicine are taken up with yaws, and with its differentiation from syphilis, to the exclusion of the larger subject as to the nature of syphilis itself in primitive peoples. Advocates of the duality of the two diseases overlook the fact that their strongest argument would be to delineate the symptoms and pathology of this pandemic syphilis which they state exists as a distinct disease side by side with yaws in tropical countries.

In spite of the importance and the desirability of a thorough study of syphilis during childhood acquired in a native people, it has never been made. In fact, Blacklock said <sup>13</sup> "What the course of acquired syphilis of early childhood may be is, and must remain, largely problematical, and a matter of speculation." Why does he despair of exact information about this form of syphilis? Why has not some one made the study of the pathology of "syphilis in a native race" which Stannus suggested?

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<sup>13</sup> Blacklock, D. B. Yaws and Syphilis, *Ann Trop Med* 26:423, 1932.

This has not been done because syphilis acquired in childhood occurs almost exclusively in those parts of the world where endemic yaws is also found. The confusion of the two diseases is too great to be unraveled. In a given case the question always arises: Is it syphilis of childhood, is it yaws, or may it be a mixed infection? Hewer<sup>10</sup> in the Sudan said that it was his original plan to investigate parallel series of cases of syphilis and yaws and to compare the results, but unfortunately it soon became clear that a differential diagnosis based on the usually accepted criteria was impossible, a definite decision could be made only by exercising one's personal prejudice. He therefore deemed it more "honest" to describe the manifestations in the whole group collectively.

Turner and Saunders<sup>14</sup> in Jamaica attempted the task of weeding out the cases of "early syphilis" from those of "early yaws," and drew tentative conclusions from 12 cases of the former which they found among thousands of the latter. The difficulties in this method of comparing the two diseases are obviously enormous.

In the discussion of yaws and syphilis the question constantly arises: What would syphilis be like if it were propagated under epidemiological conditions similar to those of yaws? As long as the Bedouins of the Euphrates Valley have *bejel* free from the venereal factor, this question can be answered, and the course of the acquired syphilis of early childhood need not remain "largely problematical, and a matter of speculation."

Blacklock<sup>13</sup> said: "The clue to the solution of the yaws and syphilis question appears to lie in syphilis as it occurs in the natives of the tropics. The effects of extragenitally acquired syphilis in the native children of rural areas of the tropics are those about which we chiefly require information."

It seems probable that a study of *bejel*, the nonvenereal form of syphilis acquired in childhood among the homogeneous and isolated group of 150 000 Bedouins of the Euphrates River valley in whom yaws does not occur, can supply the required information and furnish the required clue.

#### SUMMARY

The settled population of the Middle Euphrates valley comprises 5,000 Christians, 45 000 townspeople and 150 000 Bedouin villagers. Physical barriers separate the people of this region from the outside world and social and economic barriers separate the three groups from each other.

14 Turner, T. B., and Saunders, G. M. Report of the Jamaica Yaws Commission for 1933.

Promiscuous sexual intercourse and venereal diseases are found among the Christians to a degree comparable to that in the West. Gonorrhea, venereal syphilis (*fianghi*) and nonvenereal syphilis (*bejel*) are all found among the townspeople. Neither promiscuity nor venereal diseases are found among the Bedouins.

Syphilis among the Bedouins is called *bejel*. It is a community infection, and few persons escape the disease. The majority contract *bejel* in childhood, and the reservoir of open lesions is among the children.

*Bejel* is syphilis without a venereal factor, and it presents the unusual feature of nonvenereal syphilis in a large native population in which the disease of jaws can be excluded.

The direct comparison of jaws and syphilis has always been clouded by the fact that venereal epidemiology is either assumed in, or at any rate cannot be eliminated from, syphilis.

*Bejel*, however, is a form of syphilis that has the same epidemiology as jaws in that sexual intercourse is not concerned in its propagation. *Bejel* also resembles jaws in its widespread distribution in the community, its acquisition in childhood and the general lack of treatment.

A study of *bejel* therefore might throw light on the relationship of syphilis and jaws, since it would enable one to make direct comparison of the two spirochetoses operating under identical epidemiological conditions.

Such a study will remain possible only as long as *bejel* retains its present freedom from the venereal factor. Present-day tendencies are all against *bejel* retaining its nonvenereal character.

A scientific control in the study of *bejel* is afforded by *fianghi*, the venereal form of syphilis existing in the towns of the same region.

To label as syphilis all venereally acquired spirochetosis and as jaws all nonvenereal spirochetosis is unscientific. The use of a history of venereal infection or genital lesions as points of differentiation between syphilis and jaws is not justified.



# EVALUATION OF THE PHYTOPHARMACOLOGIC TEST OF PELS AND MACHT

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In an effort to evaluate the phytopharmacologic test which Macht and Pels<sup>1</sup> described as a diagnostic measure in cases of pemphigus, we undertook several experiments (Macht<sup>2</sup> has been reporting on the test for the past ten years and found it of diagnostic value in cases of pernicious anemia) The test is based on a comparison of the amount of growth of roots of *Lupinus albus* Hartwegii seedlings grown in a plant nutrient solution (Shive<sup>3</sup>) to which 1 per cent of blood serum of a patient has been added with the amount of growth of similar seedlings in plant nutrient solution which contains 1 per cent of blood serum from normal subjects The amount of growth retardation is taken to indicate the toxicity present in the patient's serum

## METHOD

The method used by Pels and Macht, as reported in 1931, is as follows

- 1 Seeds of *Lupinus albus* Hartwegii are soaked overnight in tap water
- 2 The soaked seeds are sprouted in ground sphagnum moss (previously washed and dried) to which water has been added to approximately 80 per cent of the weight of the moss
- 3 After forty-eight hours in sphagnum, hardy seedlings with roots of approximately equal length are selected, and the length of the roots is measured in millimeters
- 4 The roots are then immersed in a 1 per cent solution of the serum to be tested and kept at room temperature (22 C) for twenty-four hours
- 5 After twenty-four hours the roots are measured again, and the average growth is determined

In our experiments the method just outlined was followed at first, but in order that additional information might be obtained, certain modifications of the proce-

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From the Pittsburgh Skin and Cancer Foundation

1 Macht, D I, and Pels, I R Phytopharmacology of Pemphigus and Other Dermatoses Additional Studies, Arch Dermat & Syph **23** 601 (April) 1931

2 Macht, D I Phytopharmacological Study of Pernicious Anemia J Pharmacol & Exper Therap **29** 461, 1926

3 Shive, John W A Study of Physiological Balance in Nutrient Media Physiol Researches **1** 327, 1915

ture were carried out in an attempt to vary the amount of growth retardation and also to determine, if possible, the cause of it

We are using several terms in this publication which we believe need definitions to clarify them

1 The mean ( $M$ ), as used here, is the sum of all the measurements of a group of seedlings divided by their number

2 The standard deviation ( $SD$ ) is a measure of the variability or lack of uniformity of the length of rootlets in a group of seedlings. The mathematical formula used for estimating it is  $\frac{\sum d^2}{n}$ , in which  $n$  equals the number of seedlings in a group and  $d$  equals the deviation or difference of each seedling from the mean. To determine the sum ( $\sum$ )  $d^2$  one calculates the difference of each measurement from the mean, squares these differences and adds the squares. The mean  $\pm 3 SD$  has been shown statistically to include 99 per cent of all other seedlings of similar type and treatment

3 The standard error ( $SE$ ) of the mean is a measure of the reliability of the mean. This is obtained when the standard deviation of any group is divided by the square root of the number of seedlings. The standard error of a mean measures the chances that any additional seedling of identical derivation has of being accurately represented by that mean. There is a 1:1 chance that the measure of an additional seedling would lie within the quantities  $M \pm SE$ , there are four and two-tenths chances that the seedling would lie within to one that it would lie without the values  $M \pm 2 SE$ . The chances are 21:1 that the seedling will lie within the values  $M \pm 3 SE$ .

4 The plant nutrient solution will be spoken of as the Shive solution, its composition is as follows

	Cc
0.5 molar solution of calcium nitrate	10.4
0.5 molar solution of magnesium sulfate	30.0
0.5 molar solution of potassium di-hydrogen sulfate	36.0
Distilled water to make	1,000.0

#### REPORT OF THE EXPERIMENTS

*Methods Used in Sprouting Seedlings*—Pels and Macht in their experiments sprouted the seedlings in washed ground sphagnum. This we did also. Numerous tests have shown that seedlings sprouted in sphagnum and then grown in Shive's solution for twenty-four hours do not grow as long as seedlings sprouted on moistened filter paper in large sterilized Petri dishes and then grown in the Shive solution. Three hundred and thirty *Lupinus* seedlings sprouted in sphagnum when grown for twenty-four hours in the Shive solution had a mean growth of 7.73 mm  $\pm$  0.0872 SE, as compared to a mean growth of 11.26 mm  $\pm$  0.1373 SE for 464 plants sprouted on Petri dishes and grown in the Shive solution for twenty-four hours afterward. Sprouting in sphagnum conditions a lower rate of subsequent growth than sprouting in Petri dishes.

*Comparison of Growth of Seedlings of Different Plants*—The seedlings of plants belonging to widely separated groups were tested to observe their behavior and to find, if possible, a more sensitive seedling than that of *Lupinus*.

(a) Seedlings of *Raphanus* (radish) were found to be very small and super-sensitive to all sorts of laboratory conditions, many of them died and thus were found unsatisfactory for experimental handling.

(b) *Fagopyrum* (buckwheat) sprouted well in the Petri dish chamber but the roots of the seedlings when immersed sent out many side rootlets which made accurate measurement very difficult. These plants, too, were often killed in the serum solution and therefore were unsatisfactory for experimental handling.

(c) *Allium* (onion) seedlings were found to be too small as well as extremely variable in their reactions and therefore were discarded.

(d) It occurred to one of us (R. J. G.) that a rootlet normally accustomed to a hydrophytic environment might be best adapted to immersion in solutions. Therefore, *Salix* (swamp willow) cuttings were immersed in tap water. After fifteen days the rootlets were long enough for measurement and therefore for use. During the twenty-four hour test period one hundred and eighteen rootlets grew to the mean value of 0.788 mm, an amount too small for experimental purposes, and this plant was discarded.

(e) Seedlings of *Zea mays* ("white rice" popcorn) simulated those of *Lupinus* very closely. Even a larger percentage of the sprouted *Zea* seeds could be used than those of *Lupinus* because they are less affected by experimental treatment. Consequently, these seedlings were added, we believe advantageously, as test plants in many experiments.

*Variation in Growth of Seedlings of Lupinus*—The weakest point of the pharmacologic test lies in the fact that any group of plant seedlings of any particular plant species will show a striking variation in the rate of its growth. Two hundred and eight seeds of *Lupinus* were soaked in tap water for ten hours and then put into sterile Petri dishes on moistened filter paper. These were kept at room temperature for forty-seven hours and then measured. Of these seeds, forty-one did not sprout, twenty-two grew from 1 to 3 mm, nineteen from 4 to 6 mm, thirty-four from 7 to 9 mm, twenty-nine from 10 to 12 mm, twenty-five from 13 to 15 mm, fifteen from 16 to 18 mm, and twenty from 19 to 21 mm, and three grew 23, 26 and 27 mm, respectively. The mean amount of growth was 11.01 mm, the S.D. 5.9448 and the S.E.  $\pm 0.46$ . The range of growth was from 1 to 27 mm. This shows that similar seeds vary widely in their growth potentialities.

Further proof of this point is presented by a study of the amount of growth of seedlings immersed for twenty-four hours in normal (no demonstrable disease) serum solution. One hundred and ninety *Lupinus* seedlings were grown in a 1 per cent solution, forty-four grew from 1 to 3 mm, sixty-seven from 4 to 6 mm, forty-six from 7 to 9 mm, twenty-four from 10 to 12 mm and nine from 13 to 18 mm. The mean growth was 6.28, the S.D. 3.488 and the S.E.  $\pm 0.2531$ . The variation in the amount of growth was not as great as in the previous experiments. That was because only those seedlings which had attained a medium amount of growth in the Petri dishes were used, and therefore a selection of seedlings had been made. Another factor was the retarding influence of the serum solution itself. However, the range in growth rate was still found to be very great in the individual seedlings. This variability was present in all of our experiments.

At this point two questions arose. 1. Do the seedlings which attain exactly the same amount of growth during their sprouting time in the Petri dish show a highly variable rate of growth when they are grown in a solution later? 2. Does the later rate of growth vary with the rate of growth in the Petri dish? Do seedlings that are 15 mm in length when taken from the Petri dish grow more slowly in the solution than those which measure 25 to 35 mm at the end of the sprouting period?

To answer these questions a special experiment was undertaken. A large number of *Lupinus* seeds were sprouted in Petri dishes. At the end of the sprouting period, that is, in sixty hours, the seedlings which attained root lengths of 15 mm, 20 mm, 25 mm, etc., were selected and immersed in the Shive solution. At the end of twenty-four hours the seedlings were measured. It was found that those measuring 15 mm at the time of immersion grew from 17 to 35 mm in length, those measuring 20 mm at the time of immersion grew from 25 to 40 mm.

Table 1 reports that experiment and shows that the growth of all the groups after a twenty-four hour immersion in the Shive solution ranged from 2 mm to 20 mm in spite of the fact that the plants had previously shown a uniform rate of growth. The size of the plant at the end of the sprouting period does not give any indication of what the later growth of it will be. This shows that individual plants vary a great deal in their growth response, and since the rate of growth in the sprouting medium offers no clue as to the growth rate later, it is imperative that a large number of seedlings be used in each test. If a few seedlings only are used, the chances of selecting plants of equal growth potentialities are lessened, and the factor of growth potentiality has a great effect on the mean growth obtained.

TABLE 1—*Variation in Growth Shown When Plants Are Immersed in a 1 Per Cent "Normal" Serum*

No. of Seedlings	Kind of Seedlings Used	Length at Immersion	Range in Growth in 24 Hours Measured in Mm					Mean Growth
			2-4	5-8	9-12	13-16	17-20	
11	<i>Lupinus</i>	15	2	1	2	3	3	12.27
17	<i>Lupinus</i>	20	0	4	5	6	2	11.76
9	<i>Lupinus</i>	25	0	4	4	1	0	9.00
17	<i>Lupinus</i>	30	3	0	8	5	1	10.88
12	<i>Lupinus</i>	35	1	2	4	3	2	11.50
-	<i>Lupinus</i>	40	0	1	2	1	1	11.80

The fact that any information obtained from a small group of seedlings is unreliable can further be proved by the fact that the standard error is always large, showing that the mean is representative of only a small number of plants used and that the measurements obtained for most seedlings were scattered at some distance from the mean. Nineteen *Lupinus* plants were grown in a 1 per cent serum solution. They had a mean growth of 6.31 mm, a standard error of  $\pm 0.5742$ , and a range from 5.16 mm to 7.46 mm. When fifty-seven plants were similarly tested they gave a mean of 6.45 mm, with a standard error of  $\pm 0.3513$ . The probable location of the mean in this instance was between 5.75 and 7.15, which shows that even with fifty-seven seedlings one can place only an uncertain value on the mean and, further, indicates what a variable factor the rate of plant growth is.

*Effect of Different Percentages of Serum*—The effect of different percentages of serum added to plant nutrient solution was then studied. The concentrations were 0.5, 1, 5, 25 and 33.3 per cent. When sufficient serum was available, several percentages of the same serum were used, and seedlings of two different plants were imposed in parallel series. Table 2 shows these results and definitely proves that the addition of serum of any type causes a retardation in the growth of the plant and that the greater the concentration the greater the retardation becomes. When the concentration is even as high as 5 per cent, the rate of growth is so markedly

retarded, even by a normal serum, that there is little opportunity for differences in toxicity to become apparent. The difference between the various serums becomes so small as to be unreliable.

*Modification of Pels and Macht Technic*—The modification in the Pels and Macht technic was carried out in the following manner. After the experiment was concluded and the plants were removed from the serum solution, each seedling was gently blotted with absorbent paper and immersed in the Shive solution for twenty-four hours, then the growth of the plant was measured. Plants grown in the Shive solution grew 1126 mm in the first twenty-four hours and 891 in the second twenty-four hours, showing a decreased rate of growth during the second period. When plants were first grown in a serum solution and then in the Shive solution, the rate of growth was increased during the second period. After immersion in a 1 per cent serum solution, the later growth ranged around 9 mm, showing that there was a release from the inhibiting agents contained in the serum solution. After immersion in a 5 per cent serum solution the rate of growth in the Shive solution was 75 mm, after immersion in a 25 per cent

TABLE 2—*Effects of Various Concentrations of the Shive Solution*

Number of Seedlings	Kind of Plant Used	Kind of Solution	Mean Growth in Millimeters	Standard Deviation
330	Lupinus albus	Shive solution	11 26±0 1373	2.231
190	Lupinus albus	1% "normal" serum	7 72±0 2531	3.488
253	Lupinus albus	1% "pernicious anemia" serum	6 65±0 1910	2.939
333	Lupinus albus	5% "normal" serum	3 06±0 767	1.140
88	Lupinus albus	5% "pernicious anemia" serum	2 34±0 1682	1.581
520	Lupinus albus	5% "carcinoma" serum	3 84±0 0473	1.080
293	Lupinus albus	25% "carcinoma" serum	2 64±0 0447	
151	Lupinus albus	33 3% "carcinoma" serum	2 48±0 0333	0.410
198	Zea Maize (W R)	Shive solution only	9 78±0 3910	5.502
191	Zea Maize (W R)	1% "pernicious anemia" serum	4 58±0 22±0	3.110
30	Zea Maize (W R)	5% "pernicious anemia" serum	2 03±0 2810	1.5387
23	Zea Maize (W R)	5% "pemphigus" serum	5 00±0 2920	1.979
425	Zea Maize (W R)	5% "carcinoma" serum	3 60±0 0555	1.1430
265	Zea Maize (W R)	25% "carcinoma" serum	3 28±0 0450	0.7330
94	Zea Maize (W R)	33 3% "carcinoma" serum	1 09±0 0399	0.8847

serum solution, 65 mm, and after immersion in a 33.3 per cent serum solution, 555 mm. This shows that the rate of growth increases in the plants which are immersed in a serum of greater concentration, but, of course, this subsequent growth rate is proportional, that is relative, because the growth is lessened.

### CONCLUSIONS

Of a number of plants tested, only Zea mays ("white rice popcorn") was found to react similarly to Lupinus in serum solutions.

Seedlings sprouted in a moist chamber were shown to attain and maintain a more rapid rate of growth than seedlings sprouted in sphagnum or sawdust.

Tremendous variation occurs in rate of plant growth. Tests showed that apparently similar seeds vary widely in their growth potentialities.

It was shown that a mean amount of growth taken from a group of from fifteen to twenty seedlings was a very unreliable mean statistically and that therefore such a mean could not be taken as an adequate index of toxicity of serum.

It was found that plants which were of the same length when immersed in a serum solution showed considerable amount of variation in rate of growth in solution—further evidence of the unreliability of the phytopharmacologic test

By statistical analysis of the data, it is shown that as the number of seedlings for any test is increased the reliability of the mean increases

Higher concentrations of serum, 5, 25 and 33.3 per cent, have too severe an effect on the seedlings to be of any test value

Seedlings that have been immersed in a serum solution for twenty-four hours and then transferred to a normal plant nutrient solution show varying effects of the serum treatment. The effects increase with increase in concentration of the serum solution

## THERAPEUTIC TIMIDITY

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SAN FRANCISCO

Of all the members of the animal kingdom the human being is the one that comes most intimately and oftenest in contact with deleterious substances, either as medicines or in the arts and crafts. The deleterious effects of medicines have been recognized for many years. Carolus Rueus, Soc. Jesu, long ago drew attention to the Greek word *pharmacon* (hence our word, pharmacy), which sometimes meant a remedy and sometimes a poison.<sup>1</sup>

The learned, Jesuit commentator on Virgil, Carolus Rueus, stated "*Pharmacon cum ambigua vox est et modo remedium modo venenum significat*" (The word *pharmacon* is indeed ambiguous and sometimes means a remedy and sometimes a poison). Rueus, Carolus, in *P. Virgilii Maronis Opera*, edition by John Cary, London, 1835.

The physician observing the deleterious effects of medicines in his practice runs the danger of becoming overcautious, a disastrous frame of mind. This timidity is often still further exaggerated by the immense mass of literature on industrial medicine wholly occupied with the injuries caused by, and the possible injurious effects of, substances used both in medicine and in the trades.

For example, lead, which is employed as the subacetate, the carbonate or the oleate, constitutes one of the most potent remedies. That lead when ingested or inhaled, whether in solution, as in drinking water, or as a vapor or dust, as in the arts and crafts, may cause plumbism is undoubted, and that lead in its pharmaceutical forms is absorbed when it is applied on the skin there is also no doubt. Sussmann's experiments, to be mentioned later, are here positively conclusive. Therefore, it is more than theoretically possible for plumbism to occur if the medication is applied over an extensive surface and for a long time. Yet this danger must be remote, and it should not interfere with the employment of such a valuable series of remedies. For example, the bland, unctuous carbonate of lead is an excellent ingredient in an ointment for infantile eczema and is smeared over the face abundantly. As an infant's hands are always wandering over its face and into its mouth, some of the lead compound must be swallowed. Yet lead poisoning from such a source must be very infrequent. The infrequency may be

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<sup>1</sup> Pharmacal from the Latin *pharmacum*, Greek *pharmak-on*—poison or drug (Oxford Dictionary).

due, however, to the free elimination in the feces and urine characteristic of infancy

Though the actual danger of plumbism may be slight, the dermatologist should consider it, in the first place in estimating the remedy and in the second, and very significantly, to avert any excessive fear of it. Slight, however, as is the danger of inducing plumbism by the application of lead preparations on the skin one does occasionally meet with physicians willing to abandon them or to interdict their use valuable as they are

If physicians were to abandon all remedies having possible injurious by-effects they would relinquish all their most potent ones, such as arsenic. I shall not readily forget my feelings when, in 1910, in Magdeburg, Germany, I first saw arsphenamine, containing fifty times the lethal dose of arsenic, administered intravenously. It seemed to me more like an embalming procedure than a medical experience. There is no doubt that arsenical dermatitis is a grave and distressing malady, yet who would advise abandoning this wonderful remedy just because it at times acts unfortunately?

Take for example a concrete instance

Some time ago a woman consulted me on account of severe lesions of both soles caused by roentgen radiation. There were the usual tender keratoses that caused exquisite pain in walking and this was so grave as to interfere seriously with her ability to gain her living. Moreover, the lack of exercise and the depressant effect of the pain threatened permanent invalidism. Added to this was the fear of ultimate cancer, which had arrived at the point at which ablation of the sole and skin grafting were seriously considered. Even if it should be successful as a graft, this would be a desperate measure, as the sole is furnished with a special skin, and no other would be efficient. Lead is a soft, unctuous, bland heavy metal and it seemed to be the most appropriate application for the irritable condition present, so ointment of lead oleate was prescribed, together with other measures tending to improve the circulation in the feet, such as massage and bandaging of the legs. The improvement was decided. The patient was soon able to walk and stand without discomfort, and with the absence of pain and with the resumption of exercise her normally good health was restored. Of course some of the keratoses are still present, and the condition of the sole is still that of a roentgen ray burn, but the amelioration is decided.

This case is cited simply to illustrate the subject of the paper. As for the good result achieved, there was nothing wonderful in it. It was only what could be expected. The bland effect of ointment of lead oleate has been known throughout the dermatologic world since Hebra's day.<sup>2</sup> In this case it softened and soothed the painful, tender keratoses, and it would also unite with any free liquid albumin, forming lead

<sup>2</sup> Hebra, F, quoted by Richter, Paul. *Geschichte der Dermatologie*, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1928, vol 14, pt 2, p 61



albuminate, not at all agreeable to any stray parasite happening to come along to enjoy the degenerated cells

While I was congratulating myself on the improvement of the condition, a fellow practitioner suggested the probability of constitutional lead poisoning, although no symptoms were present. As I have remarked, lead can be absorbed through the skin, and inferentially may cause toxic symptoms, and in this case lead ointment was applied over a fair extent of surface, subjected to the tepid heat of the foot and each day thoroughly massaged in for hours through the action of walking. If these facts alone were considered it would appear that my colleague was justified in his fears. Against this hypothetic danger was the practical fact that ointment of lead oleate has been used in Germany as a routine treatment for sweating feet in thousands of cases. The interesting experiments of Sussmann previously mentioned cast a welcome light on this question. He found that lead in aqueous solution was absorbed through a square meter of the skin at the rate of 0.1 to 0.2 mg a day.<sup>3</sup> Incorporation in a salve greatly increased this absorbability, so that 0.5 mg ( $\frac{1}{130}$  grain) was absorbed from 0.1 square meter of skin in twenty-four hours. In this experiment the lead salve was thoroughly rubbed into the skin and then enclosed with a dressing. It was found that the addition of a soap to the ointment still further increased the absorbability.<sup>4</sup>

An important finding, however, was that the sebaceous system furnishes the gateway for this absorption. None passes through the horny layer, no matter how thin it is, and the corkscrew-shaped ducts of the sweat glands are also incapable of absorption. Atrophy of the skin together with its glands, as in scleroderma, commensurately retards absorption. From this one can see that in the case cited there could be no danger of absorption through the soles, as neither the palm nor the sole is furnished with either sebaceous glands or hairs.

On the contrary, it is interesting to note that in some countries Germany for instance, lead hair dyes are interdicted by law and that in the scalp the pilosebaceous system is extremely highly developed, furnishing the requisite gateway for absorption. Even here, however, the occurrence of plumbism may be rather an assumption deduced from the real danger present in the arts and crafts, and in drinking water delivered through lead pipes, rather than any actual danger from hair dyes.

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3 Perutz, A. *Pharmakologie der Haut*, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1930, vol. 5, pt. 1, p. 139.

4 Frey, M. V., and Rem, H. *Physiologie der Haut*, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1929, vol. 1, pt. 2, p. 6.

The lesson to be learned from the foregoing comment is that, as physicians are continually dealing with highly toxic substances administered to the most variously sensitive of all animals, they must be continually on their guard against nebulous dangers exaggerated by the abundant literature and often by their own timidity, as they might deprive themselves of the use of or cause themselves to use lamely and ineffectively, many of their most prized remedies

# AN ACNEFORM DERMATERGOSIS

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It is only within comparatively recent times that the dermatologist has interested himself in dermatoses associated with or caused by the daily work. With the advent of a more clearly defined appraisal of the words eczema and dermatitis and the more general use of the patch test, dermatologists have necessarily inquired more and more deeply into the innumerable chemical contacts that occur in the day by day lives of their patients. As well as being conversant with dermatology, the dermatologist must have a working knowledge of the manufacture and content of the many new and old compounds that are handled and applied by large numbers of persons. Hence, more and more dermatologists are becoming industrially minded, and it is dawning on them that the solution of some of their industrial difficulties may aid them in a clearer conception of the dermatoses that are encountered in their every-day practice.

Dermatargoses of the acneform type occurring in persons working with chemicals have been repeatedly reported in Europe and discussed as industrial "chlor-acne" <sup>1</sup>. This term "chlor-acne" was first used by Herxheimer <sup>2</sup> in 1899 to describe an eruption composed of comedones and small sebaceous pustules that occurred on the arms and faces of workers manufacturing chlorine gas electrolytically, using carbon electrodes. It was natural to assume that the chlorine was the causative agent. Bettman <sup>3</sup> had observed in March 1897 two patients whose skins were diffusely pigmented, dark, rough and dry in whom were observed small tenacious comedones associated with numerous small follicular abscesses. Subsequently he reported twenty-one additional cases with similar symptoms in workmen who were engaged in cleaning out an acid tower used in the manufacture of hydrochloric acid. At no time did these men come in contact with free chlorine but numerous loose

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1 White Prosser. The Dermatargoses ed 4 New York, Paul B. Hoeber Inc., 1934

2 Herxheimer. *Munchen med Wchnschr* **46** 278, 1899

3 Bettman. *Deutsche med Wchnschr* **27** 437, 1901

derivatives of coal tar were present. Heixheimer later absolved the chlorine but considered the trouble to be due to various chlorobenzenes.

From time to time other reports of the occurrence of "chlor-acne" have been made in the European journals, each author continuing the error of Heixheimer in assuming that the cause of the condition was chlorine. Some of these reports have been indefinite as to the chemical conditions under which the men worked, except that they were exposed to chlorine gas. However, some authors have suspected various chlorobenzene derivatives, such as hexa-chlorobenzene, hexa-chloroethylene, para-nitrobenzene, perchloronaphthalene ("perna") and probably others.<sup>4</sup> Chlorinated naphthalene was first indicted by Wauer<sup>5</sup> in 1918 as a cause of acneform eruptions of the skin, the condition being called *Pernakrankheit*. His observations were confirmed by Koelsch<sup>6</sup> and recently by Teleky.<sup>7</sup> The latter reported an exhaustive study of a large number of cases occurring in workers engaged in the manufacture of perchloronaphthalene, in which the workers were exposed to fumes of the molten mass and also to the sublimated dusts. In approximately one-half of the workers exposed there developed comedones of a particularly heavy and tenacious type with resultant sebaceous abscesses, containing heavy yellow pus and serum. Considerable improvement resulted when the chlorine content of the mass was decreased from 30 per cent to 8 per cent, and Teleky believed that the disease was due directly to the halogen content of the substance. He mentioned the similarity of the disease to *teeracne* (tar acne) but carried the analogy no further. Individual predisposition appeared to alter receptivity.

Some authors have leaned to the view that the acneform eruption is due to direct external contact with the chemicals (notably Bettman, Hallopeau, Jacquet, Fumouze, Teleky and Koelsch<sup>8</sup>). Others (Lehmann, Heixheimer, Jacobi, Roth and Kobert<sup>9</sup>) considered it to be a

<sup>4</sup> Occupation and Health. Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation 1925, brochures 34 and 285.

<sup>5</sup> Wauer, cited in Occupation and Health. Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation, 1925, brochure 34.

<sup>6</sup> Koelsch, F., in Ullmann, K., Oppenheim, M., and Rille, J. H. Injuries to the Skin, Leipzig, Leopold Voss, 1926, vol. 2, p. 303.

<sup>7</sup> Teleky. Klin. Wchnschr. **6** 845 (April 30), 897 (May 7) 1927, **7** 214 (Jan. 29) 1928.

<sup>8</sup> Bettman, Hallopeau, Jacquet, Fumouze, Teleky, and Koelsch, cited in Occupation and Health. Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation, 1925, brochure 285.

<sup>9</sup> Lehmann, Heixheimer, Jacobi, Roth, and Kobert, cited in Occupation and Health. Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation, 1925, brochure 285.

dermatitis due to the absorption of chemical compounds by the lungs or gastro-intestinal tract, with elimination by way of the sebaceous glands. The majority of writers on the subject particularly Prosser White,<sup>1</sup> have seemed to feel that chlorine as such has little to do with the formation of the comedones and cysts, and they have repeatedly referred to tar and products of the distillation of tar as the prime causative factors. Prosser White rebuked authors for using the term "chlor-acne" at all and expressed the belief that the process is one of the manifold cutaneous reactions produced by tar and its derivatives.

Recently we have had the opportunity to study, with the full cooperation of the manufacturers, an outbreak of acneiform eruption occurring in a group of workers engaged in the manufacture of chlorinated di-phenyl. This study has brought out some points in the production of this unusual dermatosis that we feel are important in solving its exact cause. The following case is typically illustrative of the disease as it occurred in the men working in this plant.

#### REPORT OF A CASE

*History*—O. D., a Negro aged 26, began work in the distillation of chlorinated di-phenyl in April 1930 and worked regularly until the latter part of the year 1933. About May of 1933, he noticed the appearance of blackheads on his face, neck, arms and legs. These areas itched slightly. In a short time blackheads began to appear on the chest, back and lower part of the abdomen, around the navel and on the scrotum and penis. Many of these blackheads swelled and became infected, discharging thick pus. The areas healed with difficulty and often left scars. The condition seemed to be progressive until November 1933. When seen in December 1933 the patient complained of lassitude, loss of appetite and loss of libido and said that his cutaneous condition seemed to be improving.

*Physical Examination*—On examination he seemed in good general health. His complaint of lassitude was not borne out by anything more than the usual temperament of the Negro toward work. On the forehead, extending within the hair line, and on the cheeks, chin, nose and neck were numerous small, very black, tenacious comedones, their distribution best described as being "peppered" within the skin. Many of the comedones surmounted firm shotlike cysts, which in some areas contained viscid yellow pus. The pustular elements were more noticeable on the neck. Similar shotlike comedones and cysts had appeared on the shoulders, midportion of the back and chest, with an occasional large cyst. A peculiar peppering of the skin with tenacious carbon-colored comedones was apparent around the umbilicus and lower portion of the abdomen. The scrotum and penis were involved in a similar process, the former being given more to the formation of cysts. The outer surfaces of the forearms and anterior thighs showed similar but fewer comedones. The whole eruption was acneiform but differed from acne particularly in the lack of a seborrheic appearance of the skin and in the peculiarly deep black of the comedones as well as the general peppered distribution in areas not usually involved in acne vulgaris. A general physical examination had revealed nothing of importance.

*Treatment*—He was instructed to scrub his skin thoroughly before and after his hours of work, to wear fresh clothing each day during work and to use a lotion made up as follows zinc sulfate 4 Gm., potassium sulfurata 4 Gm and distilled water to make 125 cc. On recommendation he later reported for weekly doses of roentgen radiation according to the usual manner of treating acne vulgaris.

*Microscopic Examination*—A portion of the skin of the chest was removed for microscopic study (fig 1). The chief feature of the sections was noted in the hair follicles and sebaceous glands, in which there were cystic dilatation,

*Summary of the Symptoms and Treatment in Sixteen Cases of Acneiform Eruption*

Case	Age	Race	Type of Skin	Type of Eruption	Time of Exposure	Special Treatment
1H	22	White	Seborrheic previous acne	Diffuse comedones few cysts	6 months	Incision roentg. (no therapy)
2B	28	White	Average	Diffuse comedones few cysts	5 months	None
3S	32	White	Seborrheic	Diffuse comedones, large cysts and pustules	Throughout	Incision, drainage
4W	36	White	Average dry	Diffuse comedones large cysts and abscesses	10 months	None
5F	28	White	Average	Diffuse comedones, few cysts on face and neck	Throughout	None
6S	30	White	Seborrheic, previous acne	Diffuse comedones, deep abscesses on neck severe cysts	10 months	Incision drainage
7B	20	Negro	Seborrheic	Irregularly distributed comedones, few small cysts	8 months	None
8B	19	Negro	Average	Few scattered comedones occasional cyst	5 months	None
9D*	26	Negro	Seborrheic	Diffuse comedones cysts, small abscesses	Throughout	Roentgeno therapy
10C	37	White	Average	Scattered comedones, occasional abscess	9 months	None
11G	56	White	Dry	Scattered comedones, occasional abscess	Throughout	Roentgeno therapy
12P	20	White	Seborrheic	Few comedones, occasional cyst	2 months	None
13H	37	White	Average	Occasional comedone	Throughout	None
14B	23	Negro	Average	Very few comedones	12 months	None
15F	22	White	Seborrheic	Scattered comedones	Throughout	Roentgeno therapy
16P	20	Negro	Seborrheic	Diffuse comedones, few cysts back and face	?	Roentgeno therapy

\* This case is reported in detail

destruction of the hair, marked thinning and atrophy of the epithelium of the follicles and a heavy plug of keratinized material which partly filled the cystic cavity. In some areas there was a superficial plug at the surface opening, others showed the surface open and the plug deeply situated. There was no purulent exudate. There was a zone of moderately dense connective tissue surrounding the enlarged follicles, slight edema and infiltration by lymphocytes but no leukocytes. Slight edematous changes were noted in the occasional sebaceous glands present, but they were strikingly few. The sweat glands were normal.



Fig 1—Section of skin from the chest, showing histologic changes in the formation of an acneform eruption

Of the twenty-four men working in the manufacture of chlorinated di-phenyl within the period from the late summer of 1932 to October, 1933, twenty-three were reported to have had an acneform eruption on the face and body. Of the twenty-three, sixteen were examined. These men presented eruptions of acneform character similar in type and distribution to that in the case referred to but varying in severity (table). In many patients numerous small sebaceous abscesses developed, particularly around the colloia line which exuded heavy, tenacious pus.

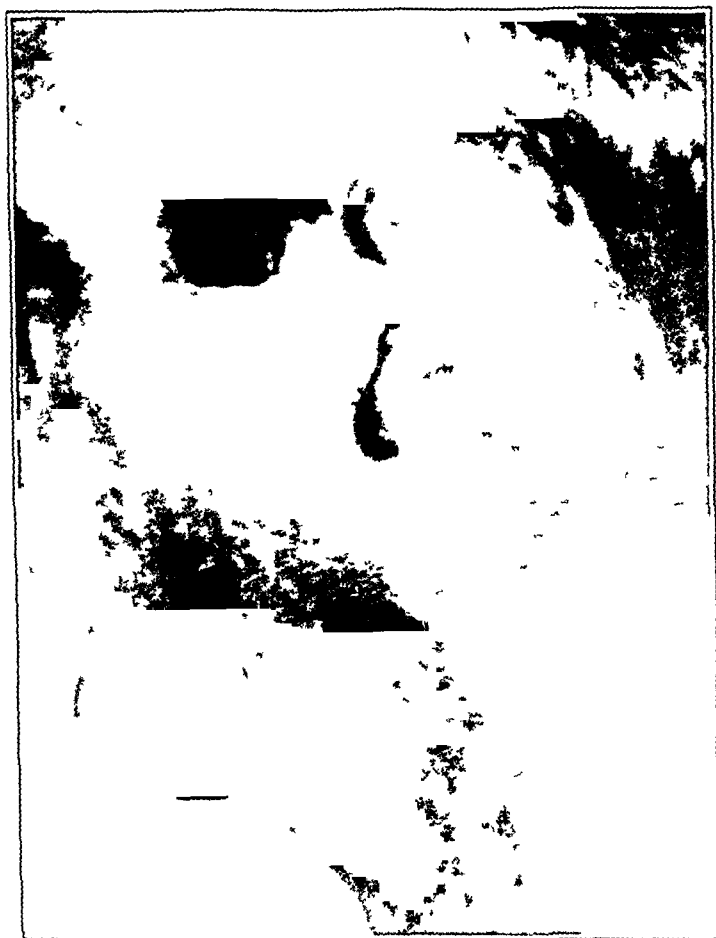


Fig 2—Characteristic appearance and location of an acneform eruption

and the remaining ulcers were indolent, leaving in their wake much scarring. In two of the cases particularly, many large abscesses developed on the neck and back.

Until very recent times di-phenyl and chlorinated di-phenyl were only laboratory curiosities, and their commercial manufacture was unknown. In the experimental stage of manufacture the apparatus was necessarily crude, and experimenters and workers were exposed for long periods to fumes and dusts containing much chlorine, both free and combined. In the early experiments, as well as in the early manufacture in large



quantities the di-phenyl was made by heating benzene derived from crude coal tar. When heated in a suitable medium benzene ( $C_6H_6$ ) becomes di-phenyl ( $C_{12}H_{10}$ ). This substance is then chlorinated at various saturation points by exposing it under suitable conditions to free chlorine gas. Distillation of the resulting chlorinated di-phenyl<sup>10</sup> results in a purified commercial product (fig 3). The commercial benzene always has a small quantity of impurities, but some of the cruder commercial benzenes contain relatively large quantities of these impurities such as xylene, toluene and paraffin. On the heating of the

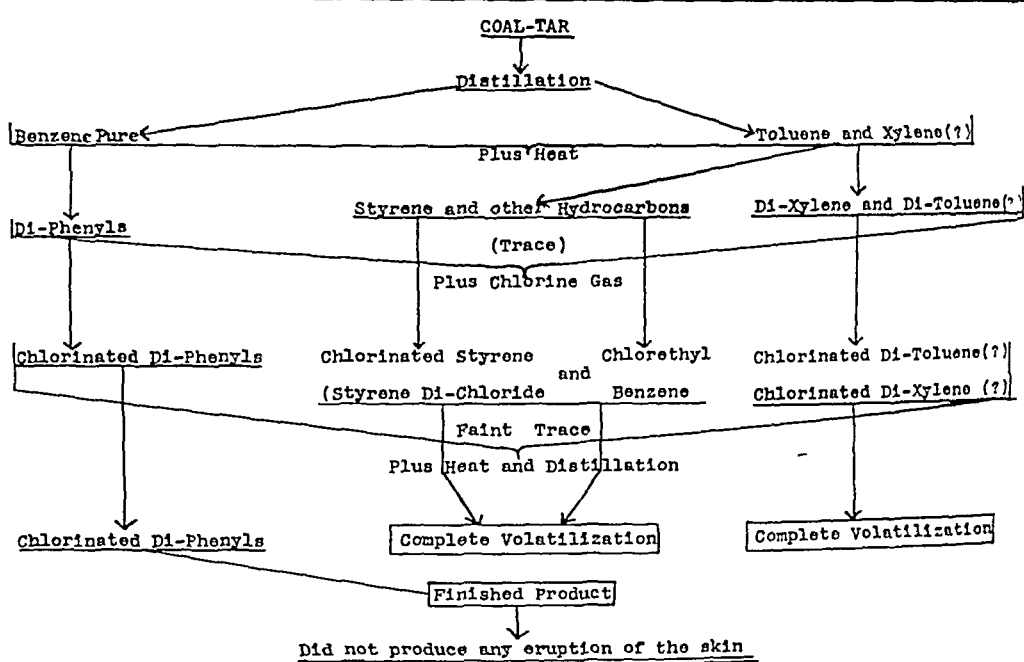


Fig 3—Chart illustrating the process of manufacture of chlorinated di-phenyl

cruder benzenes the toluenes and xylenes, when present in large quantities may produce the chemical substance styrene, which has the formula  $C_6H_5CH=CH_2$ . Styrene when chlorinated (it being inseparable from the di-phenyl) is an unstable compound dropping its chlorine atoms very readily. It is probable that other complex hydrocarbons may be formed from these impurities, which on chlorination become quite as unstable as the styrene. One of these compounds may be chloroethyl benzene ( $C_6H_5CH-Cl-CH_3$ ).

<sup>10</sup> Chlorinated di-phenyl consists of a mixture of di-phenyl chlorinated at various saturation points non- $\alpha$ -chloro-di-phenyl ( $C_{12}H_9Cl$ ,  $-C_6Cl$ ) etc

In the experimental stage and in the early manufacture of chlorinated di-phenyl, the men working were exposed for long periods to these chlorinated products. As the demand for the finished product increased, quantitative manufacture was speeded up rapidly, and open stills and heating units were of necessity used until better equipment could be designed and made. But since no physical trouble had developed in the workers previously there was no apparent hazard connected with manufacture. On or about March 1933 the electrical properties of the chlorinated di-phenyl produced in the plant the workmen of which were examined fell below the specifications, and the color of the product deepened. About one month later an acneiform eruption was observed on the faces and arms of several of the workers which became progressively worse, gradually becoming apparent among all the workers engaged in the process at that time. Although one of the men had had a slight acneiform eruption on his face in January little thought was given to it until the eruption appeared in the others. In the summer of 1932, six or eight months previous to the general outbreak of the condition, owing to a difference in price, the crude benzene was purchased from another source, and it was not until the purchase of this particular benzene was discontinued, in October 1933 that the finished product came up to the standard. During the period from March 1933 until October 1933, the eruption continued among the men and it was present as already described when the men were examined in December of the same year.

The appearance of the eruption coincidentally with the production of a poor grade of chlorinated di-phenyl seemed to indicate a relationship. On due chemical investigation styrene was assumed to be the offending substance causing the low grade of the finished product.

It seems that it may be readily assumed that our problem as to the causative agents of the acneiform eruption was connected with the chlorinated products of the impurities present in the crude benzene. However, with the exception of styrene, these products are not known. The problem hence becomes difficult of exact solution, and it is necessary to resort to a reasonable deductive hypothesis.

The exact conditions under which the men contracted their eruption cannot be satisfactorily duplicated experimentally since prolonged mild contact seems to be a deciding factor. Repeated patch tests made on numerous persons with the finished product, chlorinated di-phenyl, and the foreign substances styrene, styrene di-chloride and chloroethylbenzene, have not resulted in an acneiform eruption except in one instance. Repeated patch tests made with chloroethylbenzene in the same area produced on the third attempt an erythematous follicular eruption, which persisted only a few days but which was by no means typical.

We could not duplicate this in other instances. Since styrene, chlorinated styrene, chlorethylbenzene, xylene, toluene and their probable products are for the most part lipid solvents, they will produce death and denudation of the epithelium, and one always obtains a chemical burn in response to a patch test made with the styrene and styrene di-chloride. Small quantities mixed loosely with an inert powder or dissolved in ether produce a mild erythematous reaction but no acneiform eruption. Patch tests made with the finished product, chlorinated di-phenyl, at no time produced any erythema or evidence of irritation, hence the chlorinated di-phenyl can be absolutely absolved as an irritating agent. In looking over the consecutive history of the development of the eruption, we found it apparent that the men were in some degree exposed to the chlorinated impurities in the benzene for some time before the eruption actually appeared, and that to duplicate the conditions we should have to make repeated patch tests daily for long periods in the same person—a procedure which is not feasible.

As a group, the workers in the dusts and vapors, which were presumably saturated with chlorinated hydrocarbons, were not cleanly, making little effort to bathe after work and sweating and rubbing enhanced the liability to deposition of the substances on the skin. Theoretically, the chlorinated hydrocarbons, presumably styrene di-chloride and chlorethylbenzene, deposited on the skin gather around the hair follicles and sebaceous glands and are gradually rubbed in. Being lipid solvents, they dissolve sebum and in the reaction, which is modified by the heat of the body and the water present, give off hydrochloric acid, which causes death or irritation of the cells. This in turn causes an excess of cell growth, inflammation, sebaceous plugging and an acneiform eruption (fig. 4). This process repeated over a long period may result in severe sebaceous infection, sebaceous abscess and scarring. One would naturally expect this process to occur in the seborrheic areas as well as where clothing might rub the particles into the skin. Also one would expect the process to enhance an already existing acne vulgaris. This occurred in cases 1 and 6 (table 1) the cases in which there was the worst involvement with sebaceous abscesses.

In the beginning an attempt at prevention of the condition was made by being especially careful that all men engaged in the manufacture of chlorinated di-phenyl should have a thorough bath after working hours and that they should wear freshly laundered clothing before starting work. They were also instructed to apply night and morning veterinary white lotion to the affected parts. Some of the patients having the most numerous cysts and follicular infections were instructed to report for roentgen treatment administered in the manner usually employed in treating acne vulgaris. Following the

change in the type of benzene used and the employment of enclosed distilling apparatus and ventilation fans there was noted a gradual improvement in the acneform eruption. Those patients receiving roentgen radiation improved much more rapidly, but it cannot be said that this form of treatment gave unusual results. The final treatment of course, was removal of the patient from the offending chlorinated hydrocarbons, and then cleanliness and relief from any infection. All the men showing evidence of cutaneous disease so far as is known are greatly improved or the condition has entirely cleared except for an occasional comedo and a few scars.

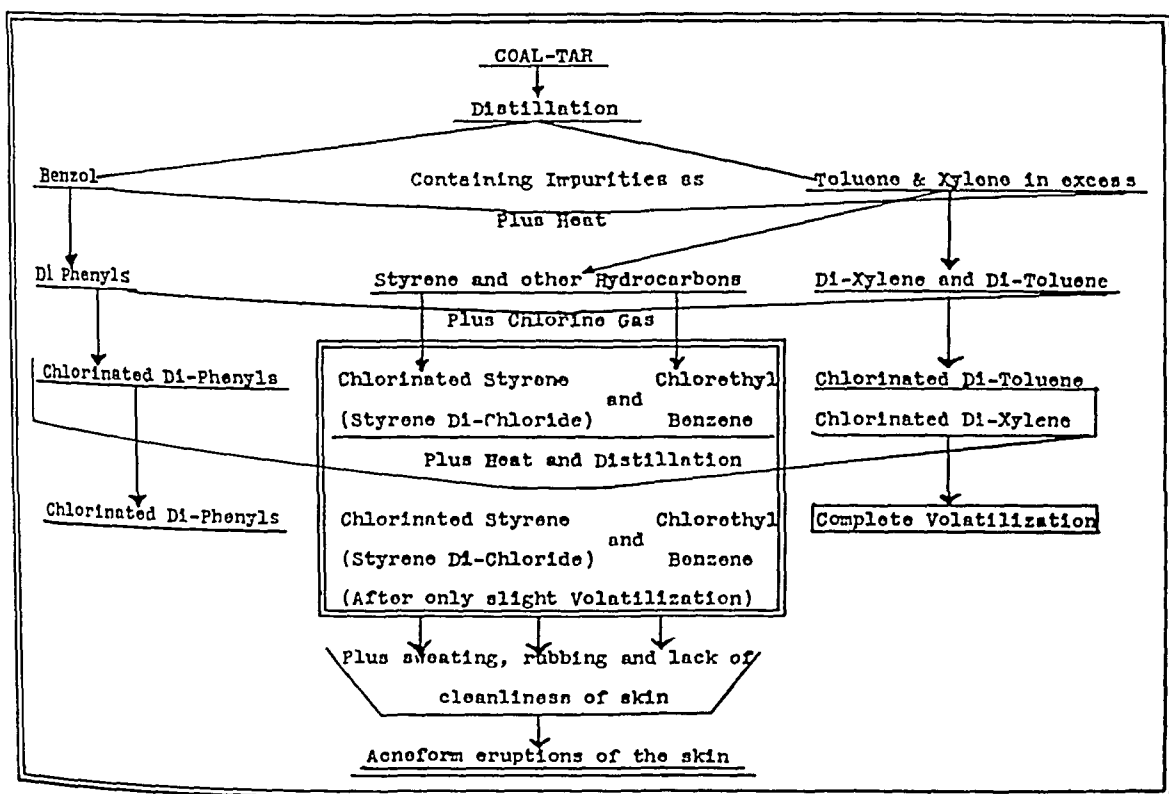


Fig 4—Process of manufacture of chlorinated di-phenyl containing impurities which cause an acneform eruption

When one recalls the cases reported by the European investigators, it is altogether plausible that the chemical process outlined here occurred in most instances. The slow liberation of chlorine in the presence of a lipid solvent (usually chlorinated hydrocarbons) was present in most cases. It is doubtful whether the disease is influenced by the quantity of chlorine present, it is apparently more due to the formation of unstable chlorinated hydrocarbons as well as to the liability of the workers to close contact without a thorough cleansing of the skin and a change from saturated clothing. It is also probable that the disease has little to do with tar itself but more with the products formed by the

chlorination of tar. Hence, the disease cannot be called "chlor-acne" or "tar acne." That it is not caused by internal absorption is evident when one considers the following facts. First, acute intoxications by chlorine rarely occur, since suffocation and death by pulmonary edema ensue even in the presence of relatively small quantities of chlorine gas in the air. Second, when ingested, chlorine and the chlorinated hydrocarbons are so rapidly oxidized and chlorine so readily combines with sodium that opportunity for acne-like eruptions, such as occur in bromine intoxication, is not possible.

In retrospect, we are intrigued by the hypothesis that these theoretical considerations may have some relation to acne vulgaris. The past quarter of a century has seen an enormous increase in the use of coal for heating homes as well as in industry. The smoke stacks of the cities have belched an ever increasing stream of coal smoke—smoke heavily laden with carbonaceous products containing numerous hydrocarbons. It is well known that coal smoke contains hydrochloric acid. Is it not possible that at least some of the acne vulgaris may have a part of its origin in the constant contacts with the chlorinated hydrocarbons of coal smoke?

#### SUMMARY

We have recorded herein observations concerning an industrial dermatosis of an acneform type. The type of eruption and the causative factors are analogous to those in the previously reported cases spoken of in the European literature as instances of "chlor-acne," tar acne or *Pennakrankheit*. Although exact duplication of the conditions under which the workers acquired the dermatosis cannot be accomplished by experimental means, reasonable deductions as to the cause of the difficulty can be made. The eruption occurred during the manufacture of chlorinated di-phenyl from benzene. The dermatosis occurred at a time when the benzene used contained excessive quantities of toluene, xylene and paraffin as impurities. The heating and chlorination of these impurities probably resulted in the production of styrene di-chloride and chloroethylbenzene, which we believe on contact with the skin produced the acneform eruption by the slow liberation of hydrochloric acid and not by internal absorption of any chemical. While many chlorinated hydrocarbons, as brought out by Prosser White<sup>1</sup> are lipid substances producing death or irritation of the cells by the liberation of chlorine, this is not true in all instances, since the finished product chlorinated di-phenyl did not either experimentally or actually, produce any cutaneous or sebaceous irritation. Irritation apparently depends on the ease with which chlorine atoms are released from the hydrocarbon base. We believe that these dermatoses should be labeled acneform dermatergoses resulting from certain unstable chlorinated

hydrocarbons and should not be spoken of as "chlor-acne" or tar acne. The suggestion has been made that some of the acne vulgaris of the skin may be the result of the same type of irritation from soot or coal smoke.

### ABSTRACT OF DISCUSSION

DR OLIVER S. ORMSBY, Chicago. I should like to add an experience I had three months ago that is of interest in this connection. I think that Dr. Jones' paper is extraordinarily interesting and valuable, and the small group of cases I am going to report may add to his troubles rather than solve any of the problems.

About three months ago in Michigan, I saw a patient, through the courtesy of Dr. Milton G. Butler, who presented an extraordinary acneform eruption. This patient was 18 years old and had been observed by Dr. Butler. The eruption in these various cases consisted of acneform pustules and comedones of variable size and depth, with scars, some of which were keloidal. The eruption occurred on the face and neck, particularly over the posterior portion, and extended well up into the scalp. The trunk, arms, thighs and legs were also involved. Two of the patients presented on the back of the neck deep perifollicular pustular lesions, with keloidal scars, such as are seen in Kaposi's dermatitis papillaris capillitii. Both deep and superficial atrophic scars, such as are seen in deep lesions leaving acne, were present in other portions of the neck, face and trunk. The comedones were prominent in all areas, including the legs. They were of variable size, and many were large and deep. The age of the affected patients varied from 18 to 50 years, the younger ones being more severely affected. The condition was apparently produced by contact with an ingredient in a fungicide produced by a chemical company for destroying fungi in lumber. The particular chemical in this fungicide that apparently was responsible for the eruption was sodium tetrachlor-ortho-phenylphenate, which is a yellow powder. Only those who came in contact with it had the eruption. Those who handled the other ingredients of the fungicide and did not come in contact with this particular chemical had no difficulty. As there were apparently no chlorine, bromine or tar radicals in the formula, it is difficult to determine the active factor in the production of the lesions and also whether the eruption was caused by local action by contact or through absorption and internal effects. The eruption was not concerned in any way with acne, and no patient in whom the eruption developed had had acne previously.

DR MARION B. SULZBERGER, New York. I think that Dr. Jones has contributed a study that will be very interesting when continued. I had an opportunity of seeing a group of patients with acne of external origin about a year and a half ago. The patients were all employed in a factory making radio condensers. Pitch tar and a type of wax (halowax, a chlorinated naphthalene) were used in these condensers. The acne which developed was like that described by Dr. Jones and also included comedones on the legs, as did that which Dr. Ormsby has mentioned. I saw six patients from this one small factory. They were all in the age of puberty or the early twenties, and the group included persons of both sexes.

I believe the most important point in this study is the possible connection between acneform dermatoses distinctly due to external irritants and true acne vulgaris. It is interesting that many derivatives of tar are closely allied to the estrogenic hormone, that certain components of tar are both estrogenic and acne-genic and that the estrogenic hormone must perhaps be incriminated in the production of acne vulgaris. There can be no doubt that acne is often due to stimulation or

irritation of the pilosebaceous apparatus and that hormonal as well as external influences can produce this stimulation. In the patient suffering from acne, who has, of course, come in contact with the estrogenic hormone during intra-uterine life and then has had no further contact with this hormone (or the closely related testicular hormone) until he or she begins to form his or her own hormones, one can readily conceive the pathogenesis of acne vulgaris as being based on an excessive stimulation of the hair follicles, a stimulation produced by the sudden new formation of the hormones at puberty. It is as though the follicles, after being sensitized to the hormones during fetal contact and then passing through a period of freedom from contact, react excessively to the new and massive contacts with the products of the gonads at puberty. I have discussed this subject in great detail elsewhere.

DR H G IRVINE, Minneapolis. I wish to comment on one point and to compliment Dr Jones on an excellent piece of work and his presentation of it. There was a difference between his situation and that which Dr Tunnachiff and I encountered (*ARCH DERMAT & SYPH* **33** 306 [Feb] 1936). In his case the manufacturers called on the medical profession to help solve the problem. Our study was undertaken where lay people were in charge. It shows clearly the need of medical advice in the production of various chemical preparations.

DR JACK W JONES, Atlanta, Ga. I am very grateful for the discussion. I did not have time to go into the various preventive measures attempted in controlling the outbreak or the treatment. In most of the cases the condition has finally cleared up.

Regarding Dr Sulzberger's discussion, we studied this outbreak and the literature rather carefully for a year and a half or two years, and we are convinced that the etiology in this particular group can be ascribed to external irritation and not to any internal complications. Our idea is that the unstable chlorinated hydrocarbons give off chlorine very easily, whereas the chlorine that is fixed in the benzene ring is comparatively stable. When these unstable chlorinated hydrocarbons come into contact with the skin and enter the hair follicles, they are broken down slowly, giving off chlorine to form hydrochloric acid. We feel that this is the primary cause of the trouble.

# ACNE AND THE CARBOHYDRATES

## PRELIMINARY REPORT

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There has long been an opinion among members of the medical profession that patients with acne vulgaris are intolerant to carbohydrates in general. Although this belief may still be held by many, there has been considerable evidence brought forward in the past decade which tends to refute such a belief.

A brief summary of the literature covering the evolution of this question from the dermatologic point of view is in order. Schwartz and his associates<sup>1</sup> reported in 1916 a series of 30 cases of acne in 50 per cent of which he found marked or borderline hyperglycemia. In 1922 Levin and Kahn<sup>2</sup> reported the results of an extended biochemical study on acne, in which they discovered no significant changes in the urea, nonprotein nitrogen, creatinine or calcium content of the blood or the dextrose tolerance. Twenty-nine per cent of 34 patients showed a value for the blood sugar content of 120 mg or more per hundred cubic centimeters, however, and 30 per cent had mild acidosis. Twenty-three patients were more thoroughly investigated, 4 of these had a decreased renal threshold for dextrose, and 19 showed fermentation of carbohydrates in the feces. At about the same time McGlasson<sup>3</sup> maintained that acne is a condition in which hyperglycemia is an almost constant factor.

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1 Schwartz, Hans J, and others. The Sugar Content of the Blood in Various Diseases of the Skin, *J Cutan Dis* **34** 159 (March) 1916

2 Levin, O L, and Kahn, Max. Biochemical Studies in Disease of the Skin. II Acne Vulgaris, *Am J M Sc* **164** 379 (Sept) 1922

3 McGlasson, I L. Hyperglycemia as an Etiologic Factor in Certain Dermatoses, *Arch Dermat & Syph* **8** 665 (Nov) 1923



A few years later, however, dissenting comments began to appear in rapid succession. Fisher<sup>4</sup> was unable to confirm the previous reports, he found hyperglycemia in but 3 of 70 patients with acne. Strickler and Saylor,<sup>5</sup> not satisfied with single determinations, computed the values for blood sugar in eighty-five specimens for 39 patients, at varying intervals. They found cyclic variations, with but 10 per cent of the patients showing hyperglycemia. They stated "A relationship may exist between the concentration of sugar in the blood and in the skin" and "This altered concentration of sugar might explain the great number of pyogenic lesions seen in certain types of acne." Pillsbury,<sup>6</sup> in studying the carbohydrate metabolism of the skin, found this organ to be a temporary storehouse for large amounts of dextrose and discovered that there are diastatic and glycolytic enzymes present in the skin. The work of these investigators also indicated that there is a fairly constant ratio between the dextrose content of the skin and that of the blood in man, although this may be disturbed following the ingestion of large amounts of sugar. A study from the angle of dextrose tolerance was carried out by Greenbaum,<sup>7</sup> who found too small a difference between his controls and his patients with acne to allow him to draw conclusions. He stated that if an intolerance for dextrose is associated with acne, it is not present in all types or even in all pustular types of this condition. This led him to believe that tests for dextrose tolerance are of no value, even if a connection exists between the intake of sugar and pustular acne or if intolerance for dextrose is part of an endocrine influence generally believed to be present in cases of acne vulgaris. McClendon<sup>8</sup> conducted studies indicating marked retention of water following the ingestion of dextrose in adults, and he expressed the belief that the skin participates in this retention of water. Rost<sup>9</sup> found no abnormal curves for the blood sugar content in cases of acne vulgaris, seborrhea or furunculosis. He felt that it is doubtful whether certain groups of cutaneous diseases are regularly connected with hyperglycemia and that therefore no disorder of carbohydrate metabolism was to be expected. In line with the work done by Strickler and

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4 Fisher, J. E. The Blood Sugar Level in Some of the Common Skin Disorders, *Arch. Dermat. & Syph.* **18** 732 (Nov.) 1928.

5 Strickler, Albert, and Saylor, M. A. Sugar Metabolism in Acne Vulgaris, *Arch. Dermat. & Syph.* **20** 705 (Nov.) 1929.

6 Pillsbury, D. M. The Intrinsic Carbohydrate Metabolism of the Skin. *J. A. M. A.* **96** 426 (Feb. 7) 1931.

7 Greenbaum, S. S. Tolerance for Dextrose in Acne Vulgaris, *Arch. Dermat. & Syph.* **23** 1064 (June) 1931.

8 McClendon, J. F. On the Relation of Blood Sugar to Blood Volume, and Carbohydrate to Water Retention. *Am. J. Physiol.* **98** 216 (Sept.) 1931.

9 Rost, G. A. Hyperglycaemia and Skin-Diseases. *Brit. J. Dermat.* **44** 57 (Feb.) 1932.

Saylor,<sup>5</sup> Strickler and Adams<sup>10</sup> made 202 estimations of the blood sugar content in 101 cases of acne and found but 10 per cent of the values to be over 110 mg per hundred cubic centimeters. In their opinion this was not more than might be expected in normal persons so that hyperglycemia could not be said to be characteristic of acne vulgaris. Changes in the values for the blood sugar content in individual cases over periods of three months did not coincide with clinical improvement or relapse. The suggestion followed that it is possible for carbohydrates to exert an indirect effect which is not demonstrable by the present types of chemical studies of the blood. In summing up these reports the statement made by Wise and Sulzberger<sup>11</sup> in 1933 seems apropos. "While clinical experience tends to show that a diet high in carbohydrates and sweets seems to make some acne cases worse, there is not an iota of scientific evidence that there is any disturbance of carbohydrate metabolism in acne."

An interesting study from the standpoint of hyperglycemia and infection is that of Tauber.<sup>12</sup> It was based on estimations of the blood sugar content in about 1500 cases, in one half of these dextrose tolerance tests were made. Of 514 persons with diabetes whose blood sugar contents averaged 197.4 mg per hundred cubic centimeters, 30, or 6.1 per cent, had furuncles, carbuncles or infections of the hands or feet. The same conditions occurred in 162 per cent of 504 patients who received medical or surgical treatment for miscellaneous infections, whose blood sugar contents had averaged 111.4 mg per hundred cubic centimeters. Two and one-half times more cutaneous infections occurred in this group although the values for the blood sugar content averaged 86 mg lower. The remaining 511 cases were all cases of dermatologic conditions. The average value for the blood sugar content in 254 patients with miscellaneous cutaneous diseases was 102.4 mg per hundred cubic centimeters, whereas an average value of but 97.6 mg per hundred cubic centimeters was obtained in 257 cases of furunculosis, ecthyma and generalized pyoderma. These findings led Tauber to treat 189 patients with furunculosis with a high carbohydrate diet, so striking that he expressed the belief that this therapy is almost a specific cure. The inference drawn was that the antibodies necessary for resistance to invasion by pus-forming organisms are provided by

<sup>10</sup> Strickler, Albert, and Adams, P. D. Blood Sugar Metabolism in Certain Dermatoses, with Special Reference to Acne Vulgaris, Arch Dermat & Syph 26:1 (July) 1932.

<sup>11</sup> Wise, Fred, and Sulzberger, M. B. The 1933 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1933, p. 10.

<sup>12</sup> Tauber, E. B. Hyperglycemia in Diseases of the Skin, Arch Dermat & Syph 27:198 (Feb) 1933.

the dextrose and the increased intake of starch. It was this piece of work which prompted the present study. It does not seem unreasonable that if furuncles were favorably influenced by such a regimen, perhaps the more pronounced and predominantly pustular types of acne would also be aided.

#### REPORT OF STUDY

It was determined that in order to carry out a carefully controlled treatment with diet and intravenous injections of dextrose the patients would of necessity have to enter the hospital rather than be handled as outpatients. Patients in whom acne was severe were not difficult to obtain. A free bed was offered, and each patient was hospitalized for a period of two weeks, during which all local therapy was withheld. A complete medical examination was made of each patient, and the usual laboratory procedures were carried out. A dextrose tolerance test was made on each patient on the morning after admission and before treatment was begun. In the ward a diet was prescribed on the following basis: protein, 1 Gm., fat, 1 Gm., and carbohydrates, 5 Gm., per kilogram of body weight. A daily intravenous injection of 1,000 cc. of a 5 per cent solution of dextrose in physiologic solution of sodium chloride was administered. Samples of urine taken during the period when injections were being given were checked for sugar, none was found in any specimen. A test of the blood sugar content after fasting was again made on the morning of dismissal. Photographs were taken on admission and again on discharge to serve as a balance against possible prejudice in the clinical estimation of the results.

The series consisted of 10 patients, varying in age from 16 to 27 years. The duration of the acne ranged from six months to ten years, in all the cases the disease was severe and predominantly pustular. Protocols of each case would shed no more light on the situation and will be omitted. In one patient the condition suggested an element of rosacea. Another patient showed almost complete involvement of the right side of the face alone. Previous therapy had included practically all types of treatment, one patient had received roentgen therapy, 22 skin units having been given over three months' time, which was completed several months before admission.

The urine was normal in all the patients, except 1, who showed the slightest possible trace of albumin in two of four specimens. The same patient exhibited pronounced secondary anemia. In all the other patients the blood counts were within the normal range. All the patients gave a negative reaction to the Hinton test. The values for the blood sugar content during fasting, at the time of admission, ranged from 78 to 92 mg. per hundred cubic centimeters and averaged 84.4 mg. The results of all the sugar tolerance tests were within the normal range, two curves were of the flat type. The values for the blood sugar content on dismissal varied from 70 to 93 mg. per hundred cubic centimeters, with an average of 80.6 mg., or about four points lower than that obtained on admission.

The results of the work are of considerable interest. Of the 10 patients, none became worse, in 3 the condition was unchanged, 2 were questionably benefited, and in the remaining 5 the condition was definitely improved. The most striking observation was the fact that the erythema associated with the larger lesions became markedly lessened; this approached blanching during the time of injection in several patients. New lesions developed in only 2 of the 10 patients during the time of their stay on the ward. 1 of these showed a few superficial papules and the other a temporary slight increase in erythema. All the patients were dismissed on the diet already described supplemented with the routine local therapy.

# Summary of Results \*

Case	Patient	Age Years	Duration of Condition	Urine	Blood Count	Dextrose Tolerance  Flat type of curve	Blood Sugar Values in Mg per Hundred Cc		Clinical Result	Length of Follow Up	Result of Follow Up
							Admission	Dismissal			
1	J R K	17	1 yr	Normal	Normal	Normal curve	87	85	Slight improvement	14 mos	Improvement continued until skin was clear
2	R L D	26	6 yrs	Normal	Normal	Normal curve	83	80	Definite improvement	10 mos	Skin gradually cleared slight pre menstrual outbreaks only
3	M A K	27	9 mos	Slightest possible trace of albumin	Secondary anemia	Normal curve	92	93	No change	Death	Death from ulcerative colitis 1 mos after dismissal
4	E C M	26	10 yrs	Normal	Normal	Normal curve	80	75	Definite improvement	6 mos	Condition stationary until roentgen therapy was given 2 months after dismissal
5	F L O	16	5 yrs	Normal	Normal	Normal curve	91	85	Definite improvement	8 mos	Skin cleared rapidly, two mild outbreaks after eating tomatoes
6	C L T H	20	4 yrs	Normal	Normal	Normal curve	86	81	Definite improvement	11 mos	Improved up 6 mos after dismissal, roent gen therapy then given
7	A R B	21	3 yrs	Normal	Normal	Normal curve	88	80	No change	10 mos	Condition stationary until roentgen therapy was given 2 mos after dismissal
8	I I C	17	6 mos	Normal	Normal	Normal curve	87	75	Definite improvement	8 mos	Skin cleared rapidly
9	J N L	20	18 mos	Normal	Normal	Flat type of curve	78	70	No change	9 mos	Skin gradually cleared
10	V P N	19	5 yrs	Normal	Normal	Normal curve	80	82	Slight improvement		Patient could not be located

\* As an immediate result of the treatment 50 per cent of the patients showed improvement in the skin was clear

\* As an immediate result of the treatment 50 per cent of the patients showed improvement In the follow up 70 per cent continued to show improvement until the skin was clear

The follow-up of these patients has extended over periods of from six to fourteen months. One patient could not be followed. The patient who showed albuminuria and secondary anemia was later found to have ulcerative colitis and died following an ileostomy. Three patients have subsequently been treated with the roentgen rays and have responded satisfactorily, 1 did well for six months before this treatment became necessary. The remaining 5 patients have continued to improve with only the high carbohydrate diet and local therapy, they are practically free from the eruption at the present time. One of these is a woman who shows no signs except a slight premenstrual outbreak, another has been troubled by two mild flare-ups, each of which immediately followed the ingestion of tomatoes. It was interesting to note that not all the last-mentioned 5 patients had shown definite improvement during their stay in the ward.

#### COMMENT

It was not expected that the high carbohydrate regimen would prove to be the ideal means of handling acne vulgaris. The results obtained in this study, however, seem to indicate not only that the old theory of a low intake of carbohydrates is inapplicable as a general measure but also that diametrically opposite treatment is often helpful.

The objection may be raised that hospitalization for a period of two weeks could of itself bring about an improvement in the average case of acne. This may be true, but the patients in this series were not bed patients in any sense of the word, they were in bed only during the time consumed by the intravenous therapy and were allowed the freedom of the ward otherwise. The fact that 50 per cent of them have continued to show improvement since dismissal also militates against the possibility that the mere stay in the hospital was a major factor.

The study of the series reported on here is but the beginning of the study as planned. A second experiment has been started in which the patients are receiving the same diet under the same conditions but in which solution of sodium chloride alone is administered intravenously. This will perhaps show how extensive a part is played by the fluid as such. As yet an insufficient number of patients have been tested to justify a report. After a study of the second series is completed other studies will be carried out, with the use of varying concentrations of the dextrose solution and also with the diet alone.

The fact that individual foods may possibly be important factors in certain cases was suggested by the report that 1 patient had two exacerbations directly after the ingestion of tomatoes. In another case there was a history of attacks which were attributed to a particular kind of home-made candy, whereas other more simple candies were innocuous. Chocolate is, of course universally recognized as a notorious offender. Specific foods have been isolated as noxious by some observers for many years. Charles J. White<sup>13</sup> as long as fifteen years

<sup>13</sup> White, C. J. Personal communication to the authors.

ago, stated that cooked fats are at fault. Recently, Cleveland White<sup>14</sup> has studied the question of specific foods in cases of acneiform eruptions. He has expressed the belief that in some of these cases the condition is based on a definite sensitization. He reported on a series of 34 patients in whom causative food allergens were determined by the use of elimination or "nonallergic" trial diets, as ordinary cutaneous tests were of little or no value. The foods most frequently found to be offenders in his cases were chocolate, milk, wheat, oranges, tomatoes and nuts. The question may arise here whether such foods may be an indirect cause of a digestive disturbance rather than primary factors in bringing about the acneiform process.

#### SUMMARY AND CONCLUSIONS

A short résumé of the literature indicates that the trend of belief is away from incriminating faulty carbohydrate metabolism as a factor in the mechanism of acne vulgaris and of furunculosis. As the first step in a study of this question, a series of 10 patients with severe pustular acne were hospitalized and given routine examinations, including the usual laboratory studies and dextrose tolerance tests, and the blood sugar content was again checked on dismissal. All the patients showed values for the blood sugar content in the lower range of normal at all times and gave normal reactions to dextrose tolerance tests. They were placed on a high intake of carbohydrates and were given daily intravenous injections of dextrose for two weeks. Fifty per cent of the patients exhibited definite improvement, 20 per cent showed a slight improvement, and none was worse. Maintenance of this diet over periods up to one year has resulted in continued improvement likewise in 50 per cent of the patients, with routine local measures as the only adjuvant. The results of this experiment definitely intimate that a high carbohydrate regimen is not inimical to the welfare of patients with acne. It is possible that other types of foods or, perhaps, specific foods, are more to be incriminated as factors in cases of acne than the long abused carbohydrates.

<sup>14</sup> White, Cleveland. Food Sensitization Dermatoses. Preliminary Report, *J Allergy* **4** 151 (Jan) 1933, Acneiform Eruptions of the Face. Etiologic Importance of Specific Foods, *J A M A* **103** 1277 (Oct 27) 1934.

# PARADOXICAL INFLUENCE OF LIGHT RAYS AS A CAUSATIVE AND AS A CURATIVE FACTOR IN CANCER OF THE SKIN

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The title of my paper requires elucidation from two standpoints. First, it is not my intent to take a definite position as to the ultimate etiologic factor in the production of cancer of the skin. Rather, I shall attempt to show to what extent radiant energy is able to produce a predisposition to the development of malignant degeneration and to demonstrate the mechanism of its activity in this direction. It is apart from my purpose to prove that the cellular damage caused by various rays is able alone to cause cancer, as it is obvious that one may be dealing merely with a soil made favorable for the development of cancer rather than with rays as an immediate causative agent.

It shall be my purpose to attempt to explain whether the paradoxical effect of light rays in the causation of malignant degeneration and in its cure is the result of different biologic effects of the rays on the cell, or whether it is the same biologic mechanism with a different end-result.

Until very recent times, this problem seemed to have been satisfactorily settled. However, in the last fifteen years, on the one hand a number of new fundamental scientific facts have appeared which have bearing on this question, and on the other hand there is an entirely new interpretation as well as regrouping of previously established facts. During the past ten years the entire theoretical structure of the biologic action of light rays has been discussed, and the conclusions have led to practical improvement in the treatment of cancer of the skin by radiant energy.

At the threshold of the discussion, one must take the stand that there is no difference in the biologic action of the various light rays. However, in the curative sense, only roentgen rays and radioactive substances come into the problem, while as causative factors not only these but the ultraviolet rays are of very great importance. Time does not permit

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Studies and Contributions from the Department of Dermatology and Syphilology, University of Michigan Medical School, service of Dr. Udo J. Wile.

me to go into minute detail as to the physical mechanism of the action of radiant energy. I shall state only that it is conceded that electromagnetic oscillations sufficiently strong split off electrons from the cell atoms. In other words, the electrons are displaced from their course near the nucleus to the periphery of the atoms. These disturbances cause a great alteration in the cell in every respect. The action of the so-called corpuscular or beta and alpha rays is in its final result identical with that of electromagnetic vibrations. Impinging on the tissues, these rays set up electromagnetic vibrations, which, in turn, reproduce beta and alpha rays.

I should like to emphasize, at this point, that the visible and caloric rays do not come into consideration in the problem under discussion. The reason for this is that the quanta of these waves are not large enough to split off electrons from the atoms and to displace them to the peripheral courses of the atoms.

The size of the quantum of the caloric waves, taken as a unit, establishes the ultraviolet quantum as two or three times higher. Depending on the wavelength, the quantum of roentgen rays is from 720 to 70,000 times higher than the caloric unit, and that of gamma rays, 720,000 times higher.

The quantum of the caloric rays, therefore, is not sufficiently strong to exercise a substantial effect on the atom. The caloric rays, therefore, may be considered only as a physical remedy causing destruction by actual heat. In this sense, they are unimportant either as immediate or remote factors in the causation of cancer of the skin. When, under unusual circumstances, cancer occurs following a burn or a therapeutic burning procedure, it is analogous to that occurring in scar tissue and in no way is associated with the cancer induced by radiant energy. Cancer never occurs following such therapeutic procedures as diathermy, unless actual burning has taken place. The same thing is true of the so-called kangri cancer, which starts from a scar as a result of a burn and is not analogous to cancer occurring after physiologic and pathologic irradiation.

I am concerned, therefore, only with ultraviolet rays, roentgen rays and the rays of radioactive substances. These all work in the same manner, differing only in the strength of the effect produced. The differences of these effects are determined, first, by the size of the quantum and, second, by the difference in the absorption of the rays by the tissue affected.

These facts established, I must discuss the changes produced in the tissue by such radiation. Two questions present themselves for elucidation. First, do all tissues react in a similar way to radiation of the same strength, or is there a qualitative difference in their reaction?



Second, do differences in the strength of the same radiant energy exercise the same or different effects on the same tissue?

With regard to the first question there is unanimity that in any tissue the biologic effect will vary only in degree. It is only in this variance in degree that one can speak of an elective biologic effect on tissue.

With regard to the second question there is still wide divergence of opinion.

According to the so-called law of Arndt and Schulz, a very small dose of radiation exerts a biologic action different from that of a large one. There are many who still support this view.

The interpretation of Arndt and Schulz bears directly on the salient point of the paper in relation to the causative versus the curative effect of radiation. Small doses of radiant energy distributed over a long period would in this sense act as a causative factor, while the large doses required in the treatment of cancer of the skin would act as a curative agent. If, therefore, the Arndt and Schulz theory is true for the biologic effect of radiation, there is a true paradox in the action of light rays in both curing and causing cancer and not a paradoxical end-result alone.

The explanation of Arndt and Schulz presupposes that small doses stimulate functional activity of the cell, whereas the higher doses paralyze these functions and still higher ones result in cell death.

There is considerable confusion when one reads the German literature as to the interpretation of the word *Reiz*. This word implies both stimulation and irritation. There is no question that irradiation spells irritation for the cells. The real question for discussion is whether a small dose of radiation can cause stimulation in the sense of increased functional activity. Before carrying this discussion further, it is proper to note that the law of Arndt and Schulz, stated first on pharmacologic grounds, is disputed by such eminent authorities in pharmacology as Meyer and Heubner, and the roentgenologic accuracy of this observation is especially questioned by such authorities as Holzkecht and Pordes.

The literature of the last ten years on the subject seems to favor the views of Holzkecht and Pordes<sup>1</sup> that, so far as roentgen rays and gamma rays are concerned, stimulation of cells does not take place. It is more difficult to take a positive view with regard to the effect of ultraviolet rays, since constant irradiation with these occurs in the natural environment, and it is therefore difficult to determine what constitutes an additional dose.

<sup>1</sup> Holzkecht and Pordes. *Strahlentherapie* 20: 555, 1925.

It is known that the lack of such rays causes underdevelopment. Thus, certain salamanders living in the darkness of caves are not pigmented and are sightless. When, however, these animals are exposed to light they acquire pigment and organs of vision. This can hardly be attributed to a stimulation in the pathologic sense but merely to the development under the influence of light to a normal state. In this connection, there are some interesting experiments on the increase in growth of plants under irradiation. Reiss<sup>2</sup> determined that following irradiation there was an increase in the development of the buds of the lilac. He found, however, that this increase was merely an increase in water content. He was not able to determine any marked increase in cellular activity or in number of cells. The experiments, however, of Schwarz,<sup>3</sup> Guillemot<sup>4</sup> and others along similar lines seem to suggest that under irradiation there is increased cellular proliferation. Of great interest are the experiments of Weber,<sup>5</sup> who found that by irradiating lilac buds they could be made to bloom much earlier, but the plant rapidly perished. In like manner, the irradiation of frogs' eggs and the bones of young rabbits and dogs by Hoffmann<sup>6</sup> resulted in a much more rapid cellular development, which, however, was very temporary, as controls had caught up with the experimental material within two or three weeks. The analysis of these findings suggests in the one instance an increased cellular activity owing to irradiation which rapidly led to cell death, as in the experiments on the lilac. Other experiments seem to indicate a temporary stimulation of cellular activity, but the cessation of this activity after increased growth and a relapse to normal growth suggest cellular injury, the occurrence of which I hope to prove later.

It is incontestable that irradiation may have the effect of increasing the proliferation of the cancer. This is a common experience. Ritter and Lewandowsky,<sup>7</sup> for example, treated the cutaneous metastasis of ovarian cancer with various doses of roentgen radiation. They described a proliferation following the application of small doses and a disappearance after large ones. I have emphasized the importance of this in a book by Bohmer and myself,<sup>8</sup> "Light Treatment in Cutaneous Diseases," by stating that in the irradiation of malignant tumors it is necessary to give a dose large enough to destroy the tumor tissue. If

<sup>2</sup> Reiss Compt rend Soc de biol **92** 987, 1925

<sup>3</sup> Schwarz, G Arch f d ges Physiol **100** 532, 1903

<sup>4</sup> Guillemot Encyclopédie scientifique, Paris, Dom et fils, 1910

<sup>5</sup> Weber, Friedl Arch f d ges Physiol **198** 644, 1925

<sup>6</sup> Hoffmann Strahlentherapie **13** 285, 1922, **14** 516, 1923

<sup>7</sup> Ritter and Lewandowsky Strahlentherapie **4** 412, 1914

<sup>8</sup> Blumenthal, Franz, and Bohmer, Lothar Strahlenbehandlung bei Hautkrankheiten, Berlin, S Karger, 1932

one gives less than this dose one frequently sees an increase in the growth in both width and depth, and this is so common that it cannot be regarded as a coincidence

This phenomenon, however, is explainable on grounds other than direct stimulation of the cancer cell Gatenby,<sup>9</sup> for example, following irradiation of tumors with one one-hundredth erythema dose observed cessation of mitoses in the cancer cells and appearance of abnormal mitoses The increase in growth of a malignant tumor following underdosage can therefore be ascribed to the effect of proliferation of the remaining cancer cells caused either by the irritation and inflammation arising in the subcutaneous tissue or by the irritation exerted by the death of certain of the affected cancer cells, rather than by the stimulation of the light rays

I do not believe that there are any experiments which prove conclusively that there is a distinct biologic difference between the primary effects of small and large doses on the individual cell My own view is that both small and large doses inflict an initial injury The initial injury under small doses produces changes which, in some instances, simulate cell stimulation The effect of irradiation in relation to dosage differs, then, only in degree, the larger doses producing cell death, the smaller ones provoking cellular disturbances which in effect are inimical to the further normal existence of the cell Here one must distinguish the cell from the organism as a whole The effect of small doses on cellular activity of certain types—for example, that in psoriasis—is inimical to the cell but beneficial to the host, and it is in this way that the therapeutic effects of small or divided doses of roentgen radiation are explainable

I can now enter the discussion of the causative factors in the production of cancer as they refer to light rays on the one hand, and the curative potentialities of light rays, on the other

In what manner does radiant energy or do rays of light affect the activity of cells and tissue? In this connection, there are some interesting experiments with protozoa and lower animal forms These experiments concern themselves not with the immediate effect of irradiation but with its ultimate results There is, of course, a latent period between irradiation and the first appearance of change There has been great dissension as to the manner in which the cell is injured by irradiation It is now definitely established largely through the work of Hertwig<sup>10</sup> and of Halberstaedter,<sup>11</sup> that the nucleus is the chief point of injury

9 Gatenby *Irish J M Sc* 48 748, 1929

10 Hertwig *Strahleneinwirkung auf Wachstum und Entwicklung*, in Lazarus P *Handbuch der gesamten Strahlenheilkunde*, Munich, J F Bergmann, 1927, vol 1 p 444

11 Halberstaedter, L *Berl klin Wchnschr* 51 252 1914

The question at issue, however, is first whether the nucleus is directly injured by light rays, or whether it is secondarily changed by the immediate injury to the protoplasm. Working with trypanosomes, Halberstaedter determined that the first injury to the cell from irradiation is in its generative function that is to say, its ability to divide. This was later shown in the frog egg by Hertwig. There are, of course, many other changes which occur in the cell from irradiation. For my purposes, the change in the power of regeneration is of especial interest. Hertwig and Muller working independently, demonstrated that irradiation of both the egg and the spermatozoa of the frog produces no apparent structural change but results in a very large number of deformities. From these experiments Hertwig concluded that the function of differentiation of a cell is disturbed if its nucleus is harmed.

It is just such differentiating cells which one finds in the basal layer of the epidermis. These cells perform all the work of differentiation as well as that of regeneration of the epidermis. In this layer and in the changes which take place following irradiation one must look for the understanding of the point under discussion, namely, the curative and causative factors due to the action of rays in relation to cancer of the skin. In connection with the causative effect that is to say the changes that take place in the basal layer which lead directly or indirectly to cancer, it is best to consider at first the ultraviolet rays, and of these the so-called Dorno rays, or rays of 3 000 angstroms, are of the greatest importance for discussion. I omit for the present notice of the action of gamma rays and roentgen rays, and turn to the ultraviolet rays for the reason that in the application of roentgen and gamma rays there are added factors in injury to the subcutaneous tissues and blood vessels. Bachem demonstrated that 66 per cent of ultraviolet rays is absorbed in the superficial layers of the epidermis and that the basal layer and the cutis each absorb about 16 per cent. From this it is possible to see the definite protective function of the horny layer against these rays.

Ultraviolet rays in doses surpassing the physiologic limit produce characteristic changes in the basal cell layer. According to Miescher,<sup>12</sup> the damaged cells show all the signs of pathologic karyokinesis. After two or three days these cells can be seen in the horny layer, where their nuclei are retained. At the very outset leukocytes are seen emigrating from the cutis into the epidermis, but this mild infiltration is not sufficient to produce the changes mentioned, which are without doubt the effect of the rays acting on the nuclei of the basal cells. The greatest emphasis must be put on this point. It is known that the basal cells produce two protective measures against the rays: horny substance as a product of the nucleus and pigment as a product of protoplasm.

<sup>12</sup> Miescher, G. *Strahlentherapie* 45 201, 1932.

Certainly it is not accident that the most impressive changes in precanceroses due to radiation are found as hyperkeratoses and hyperpigmentation and that developing cancer finds its starting place in tissue so changed. In this fact one again meets an apparent paradox. The very reaction of the cell as a protective measure against the rays seems at the same time to be the starting point for cell degeneration.

Kyrle<sup>13</sup> took the view that pigmentation and hyperpigmentation are functions purely protective against the ultraviolet rays, and he further regarded keratinization and hyperkeratinization as in no way concerned with the defense mechanism against the rays. According to his view, proliferation and pigmentation are not coordinate, but proliferation follows pigmentation. He advanced the idea that those cells which have lost the power to produce pigment give all their strength to proliferation. I cannot agree with this view. It is well known that pigmentation and thickening of the horny layer are both protective mechanisms against the rays, the immediate thickening of the horny layer in fair and red-haired persons exposed to ultraviolet rays is so impressive that it overshadows the protective mechanism of the pigment. The importance, however, of the pigment is clearly indicated in the fact that the Negro's skin is ten times less sensitive to ultraviolet rays than the white person's skin. Pigmentation and keratinization are definitely coordinating functions of a mechanism protective against these rays.

If the cells of the basal layer receive a quantity of radiant energy exceeding physical limits, a third process starts, and this is a degenerative one, just such as occurs in eggs and spermatozoa following irradiation. This degeneration is not a result of increase of pigment, nor is it due to proliferation of the epidermis, but it is due to an inherent loss or lack of a protective function. Statistically, people lacking in pigmentation or more exposed to ultraviolet rays are found with the highest percentage of cancer of the skin. This is evidence in support of the fact just stated.

Statistics have shown that cancer of the skin in the majority of cases is localized in those places exposed to ultraviolet rays. Red-haired and fair persons having occupations which expose them to these rays are definitely predisposed.

I state it as my belief that the degeneration in the epidermis starts very early following irradiation and that the continued application of small doses leads ultimately to visible changes in the skin until finally malignant degeneration takes place. The developing neoplasm occurs in the places of greatest proliferation, therefore it always begins in a wartlike hyperkeratosis which it is perfectly proper to characterize as a precancerous change.

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<sup>13</sup> Kyrle. *Vorlesungen über Histobiologie der menschlichen Haut und ihrer Erkrankungen*. Berlin Julius Springer 1925 vol. 1.

From the clinical standpoint, the changes in the skin affected by various types of rays give a very uniform picture. They differ materially only in the element of time or duration and the saturation of the insult.<sup>14</sup> The changes seen after a lifetime of exposure to sunlight are in no way different from those produced by a single overdose of roentgen radiation, and the reaction to the insult will differ markedly according to the race and color of the subject, but only in degree. Thus, the senescent changes due to saturation with sunlight occur in blonds much earlier than in darker persons, and they occur at an extremely early age in those patients who have a congenital defect in their resistance to light.

It remains for me now to discuss the question, In what manner does a precancerous change develop into cancer of the skin?

Bordier,<sup>15</sup> on the basis of a very large clinical experience, stated that a cancer develops from a precancerous lesion not only as the result of a continuation of the initial insult but as a result of any continued trauma. This fact is extremely important because the transformation from a precancerous lesion to cancer does not require the same insult which initiated the lesion. Any irritation or casual trauma can act as the determining insult. Cancer develops from arsenical keratoses in which the arsenic as the initial factor in the development of the hyperkeratosis has long ceased to exist, and the cancer usually ensues from an external traumatic source. The same thing is occasionally seen in cancer caused by roentgen radiation. The first stage is initiated as precancerosis by the rays, the final stage is initiated by friction of clothing or other casual traumatic incidents. The salient point in this discussion is that ultraviolet rays do not cause cancer in themselves. They produce characteristic degenerative and regenerative cell changes leading to precancerous lesions in the skin. With such changes in situ, any irritation, including additional ultraviolet rays, can cause the precancerous change to become malignant. It must be admitted that only a small number of precancerous changes, even those subjected to continuous trauma, undergo malignant degeneration. Expressed otherwise, all persons with precancerous changes do not necessarily acquire cancer. For this reason, one must assume another factor, which does not come within the realm of this paper for explanation, but which is of great importance, namely, a predisposition or an inherent tendency to malignant degeneration which must be based on the factor of constitution.

<sup>14</sup> As Dr W. A. Pusey pointed out [Science **33** 1001 (June 30) 1911], radiant energy gives an exaggerated picture of the senile skin, and the starting point for the cancer in both conditions is situated in the keratoses. He stated the belief that the senile changes of the skin are in good part the result of the less powerful action over a long period of years of sunlight.

<sup>15</sup> Bordier. *Paris méd* **1** 109 (Feb 4) 1933.

I now come to the mechanism of healing which follows irradiation, and here again there are two explanations offered for the disappearance of cancer cells under the influence of radiant energy. On the one hand, Opitz,<sup>16</sup> Theilhaber,<sup>17</sup> Frankel,<sup>18</sup> Ricker<sup>19</sup> and others have expressed the belief that the disappearance of cancer cells is indirectly due to changes in the connective tissue of the stroma. They have held that the death of the cancer tissue is not a direct action of the rays but results from secondary changes affecting the connective tissue as well as the blood vessels. Some are so convinced of this that they believe it unwise to use such doses as may injure irreparably the protective mechanism of the connective tissue.

On the other hand, and directly opposing this view is that held by the majority of observers that death of the cancer cell is directly due to the action of the rays on the cancer cell itself. If this view is correct, the production of cancer by radiant energy and its cure by the same agent occur by the same mechanism, as between the degenerative and the lethal effect there is merely a difference of degree. Therefore, the same physical mechanism leads to a paradoxical end-result.

A great many clinical and histologic researches are concerned with this particular question. From the clinical standpoint, it is always the experience that cell death in cancer of the skin results only from the application of large doses of radiant energy, and that disappearance and cure never occur following small doses. This speaks for the necessity of direct action on the cancer cell to insure its death and the cure of the lesion. These clinical findings are in complete accord with the histologic pictures in cancer tissue which has been irradiated. It is an accepted fact that the most striking changes first seen occur in the nuclei of the cancer cells. The nucleus falls to pieces, karyorrhexis, karyolysis, giant nuclei and giant cell formation and vacuolation characterize the picture. One finds vacuoles, edema, lipoid degeneration, small hyaline bodies, granulation and lysis of the protoplasm. In short the cancer cells show all phases of degeneration. Without question, the stroma is also changed but not in such degree that one could in any way explain the cell degeneration as subsequent to it or caused by it. In this connection, Perthes<sup>20</sup> has shown that changes in the cancer cell can be demonstrated before any change takes place in the connective tissue.

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16 Opitz *Monatschr f Geburtsh u Gynak* **61** 232, 1923

17 Theilhaber, A. *Strahlentherapie* **11** 686, 1920

18 Fränkel *Zentralbl f Gynäk* **44** 1285, 1920

19 Ricker *Strahlentherapie* **5** 679, 1915

20 Perthes *Strahlentherapie* **14** 738 1923

That the connective tissue changes are secondary or come as a later event following irradiation is the final conclusion of Lubarsch and Waetjen,<sup>21</sup> who have published an extensive monograph on the subject.

One may conclude, therefore, that the degenerative effect of radiant energy, which on the one hand leads to the development of cancer tissue and on the other to cure of the same tissue which it provokes, constitutes a true example of a paradoxical fact in medicine.

Differences in the dose and in the method of administering the rays lead to quite different end-results, small repeated doses lead to senescent changes such as farmer's skin, xeroderma pigmentosum, roentgen-ray dermatitis and radiodermatitis, all conditions concerning the precancerous nature of which there is no doubt. On the other hand, large doses lead to the cure of cancer. Small doses lead to a morbid condition of the cell and large doses to death of the cell. Still more paradoxical, it seems to me, is the fact that a massive dose intended to destroy cancer may produce cancer in the area irradiated. I cite here an experience of Dr. Wile's. A woman, following amputation of the breast for cancer, received a large dose of roentgen radiation to the axilla. She remained free from any appreciable effect for fifteen years. After this time, telangiectasis and hyperkeratoses developed rapidly and quickly led to malignant degeneration. This paradoxical end-effect may be explained on the basis which I have set forth already. It is known that in irradiation not all cells are injured to the same degree. The cells in the process of mitosis and in that immediately following it are the most sensitive. The remainder, apparently slightly or not at all injured, take part in the regenerative process. They have received, however, more or less of the degenerative injury, which is responsible for the later visible degenerative processes in the areas injured, and these later lead to cancer.

#### CONCLUSIONS

1 I believe that in irradiation the mechanism acting on the cells exercises paradoxical end-effect in the development of cancer on the one hand and its cure on the other.

2 In both these processes, one is concerned with a degenerative effect in the cell particularly affecting its nucleus.

3 Dependent on the degree of the irradiation, ultraviolet rays, roentgen rays and rays of radioactive substances behave in exactly the same manner whether they lead to repair, to permanent degeneration and hence to malignant degeneration or to cell death resulting in cure of the cancer.

<sup>21</sup> Lubarsch and Waetjen. Allgemeine und spezielle Histologie der Strahlenwirkung, in Lazarus, P. Handbuch der gesamten Strahlenheilkunde, Munich, J. F. Bergmann, 1927, vol. 1, p. 304.



# J FRANCIS AITKEN

## AN APPRECIATIVE SKETCH

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This paper does not pretend to be a biography, an obituary or a eulogy. My sole reason for its presentation is my deep affection for Aitken, which has extended over many years, and I hope that I may make him seem real to those who did not know him and refresh the memories of those who knew him well.

In many respects Aitken was an extraordinary person. He was a member of no dermatologic society other than the Section of Dermatology and Syphilis of the New York Academy of Medicine, the sessions of which he attended irregularly and only as a listener. He refused all offices and did little, if any, writing, yet he was considered one of the most eminent clinicians in New York and second to none in diagnostic ability. In my opinion, based on intimate contact with him for twenty years, this seeming neglect of the higher things in dermatology was due entirely to an innate modesty and diffidence; he hated the limelight to such an extent that he could not be induced to air his opinions in public, but in his own circle of intimates he did not hesitate to venture his views, and they always proved of great value. Aitken was highly intelligent, with great reasoning ability and a marked degree of common sense. This combination of qualities, together with the personal inspection and therapeutic direction of, conservatively, some 10 000 patients a year for forty-four years, developed him into a master clinician, with a thorough knowledge of the many-faceted variations of the commoner dermatoses.

It must be difficult for the younger dermatologists to realize the diagnostic ability and therapeutic results attained by the pioneers of yesterday. These eminent dermatologists made up for their lack of laboratory facilities with unusually trained analytic and photographic minds together with exhaustive clinical notes and an extraordinary development of what might be called sight diagnosis and what I sometimes call the sixth dermatologic sense. Jonathan Hutchinson is a good example of a physician with this peculiar gift, as is also Alfred Fournier. Their therapeutic results were surprisingly good. The old-fashioned curet, the electric needle, the cautery point, the comedo extractor and

even an ointment accomplished results which would surprise and even astound the fledgling dermatologist of today, accustomed as he is to the innumerable paraphernalia of the modern dermatologist's office

Of all the physicians who have served the New York Skin and Cancer Hospital, I believe that I can say, without fear of contradiction, that J Francis Aitken gave more of himself in its service than any one else. He was house physician from Dec 1, 1883, to Dec 1, 1884, and thereafter became, successively, clinical assistant, assistant physician and attending physician, he held the last position until a year or so before his death on Aug 3, 1930. Therefore, for forty-four years he attended the hospital three days a week, and during the twenty years that I knew him he never failed to be present at 2 p m, never missed a day, other than a few weeks in the summer, always faithfully made his rounds and attended meetings of the Medical Board, and this in all kinds of weather, no matter how ill he might have felt at times. Such was his service, and in my estimation it deserves far more recognition from a hospital than the greatest of financial contributions. Such a record deserves to be emblazoned to high heaven and serve as an example to all physicians.

Aitken was born on Oct 28, 1851, and graduated from the Bellevue Medical College on March 14, 1883. He was the first to serve as house physician at the New York Skin and Cancer Hospital. When he became the only member of its house staff the hospital had been in existence for almost a year, as it was opened on Jan 11, 1883. The entire staff consisted of L Duncan Bulkley and George Henry Fox as attending physicians and Daniel Lewis and W T Alexander as assistants. A special department for internal cancer in females was in charge of J B Hunter and J D Anway. In the first year 774 patients were treated, including 49 with cancer. This was the cradle of Aitken's dermatologic life. It was here that he developed the diagnostic acumen which we admired so much. He was probably the greatest exponent and propagandist of sight diagnosis in dermatology whom I can recall. I have frequently heard Fred Wise express the wish for the return of sight diagnosis as taught by Aitken in preference to complete dependence on laboratory reports. Aitken always made a diagnosis first, he disliked having any one question the patient until all had expressed an opinion. Such a method naturally stimulated his keenness of observation, and that was exactly what he always tried to inculcate in all his associates. He occasionally "muffed" a diagnosis, as he was the first to admit, but his accuracy, on the whole, was phenomenal. Even at times when his subordinates thought that he was wrong, time proved him eventually right. He liked to surround himself with his staff and make every one, even the youngest intern, offer a diagnosis and then patiently point out the many mistakes that we had made.

He was especially fond of the diagnosis *pityriasis maculata et circinata*, which, as may be surmised, is better designated as *pityriasis rosea*, yet in the use of the former term he had distinguished company, for both Bázín and Hardy used it in describing *pityriasis rosea* long after Gibert had given it its proper name. He resented most being told the latest theories by the youngest "know-it-all," which is so common in every clinic, at such times, particularly if it had been a hard and hot afternoon, he would literally explode.

After all the patients had been seen he often regaled us with tales of old New York. In his younger days he was fond of horse-racing, and he always drove a handsome pair of bays. He had a convivial nature and often spent an afternoon or evening at the old Hoffman House or some other well known hostelry with such old cronies as Stuyvesant Fish and Stanford White.

I believe that it was during Aitken's incumbency at the clinic that a woman suffering from chronic eczema misunderstood the instructions and swallowed a teaspoonful of calamine lotion three times a day for a week and at the same time generously patted on the eruption her rhubarb and soda mixture. On her return after a week of this bizarre treatment, instead of presenting alarming signs of phenol poisoning, she seemed greatly improved, whereupon an ointment containing 4 per cent rhubarb was used for many years in the clinic in the treatment of eczema.

Aitken was stout and florid. On hot days great beads of perspiration stood out on his forehead. He always was in shirt-sleeves and occasionally wore vivid-colored garters on his arms. He always carried the largest magnifying glass that I have ever seen, through which he peered at the patients and with which he would scare the wits out of them when he was especially vehement.

Aitken sought no honors. He did not even get an appointment as Attending Physician at the hospital until 1912, thereby serving twenty-eight years as an assistant, despite his great ability and faithful attendance. He invariably referred to a superintendent who took herself most seriously as "the Matron," much to her obvious disgust. Aitken always remained aloof from hospital politics, and when he did take sides it was always for justice's sake. He was guileless, and his rough exterior covered a great heart.

He practiced in the same location on East Thirty-Fifth Street for more than fifty years, and in that time he brought comfort and relief to many sufferers. I remained at his elbow for twenty years, and the proudest moments of my life were when he called me "son," which he frequently did in his later years. J. Francis Aitken lived and died fearlessly. He loved life, his specialty and his fellow-men. Need more be said other than that we who knew him best loved him most?

# CURABILITY OF SYPHILIS

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Theoretically and practically syphilis is curable. However, it is impossible to decide when the last spirochete has been eradicated in the individual patient. This question is nevertheless of grave moment to the community, to the infected person and to the physician. Under modern conditions clinical and serologic "cure" is readily obtained in most instances. Radical biologic cure with complete destruction of the last spirochete is a therapeutic ideal which probably is attained frequently when intensive and continuous therapy is used during the early stages of the disease, especially in patients with primary syphilis, whose serologic reactions are negative. At present there is no reliable test for the determination of the presence or absence of the spirochetes in the human body. The various serologic tests merely indicate a reaction on the part of the body against the spirochete. When these tests are negative there is no proof that the spirochete is not present in a state of latency. There is a tendency to relapse after any plan of antisyphilitic therapy. Stokes and his associates<sup>1</sup> have reported the incidence of cutaneous and mucous relapses as 96 per cent in patients with an early stage of syphilis who received treatment with arsphenamine and as 36 per cent after the use of arsphenamine and a bismuth preparation. Persistently positive Wassermann reactions were recorded in 66 per cent of patients with primary and secondary syphilis and in 22 per cent of those with latent, late and hereditary syphilis. Latency is a peculiar characteristic of the infection. It has been demonstrated at necropsy that a patient without clinical symptoms and with a negative serologic reaction may harbor intact spirochetes. Warthin<sup>2</sup> studied cases of such "cures" and found spirochetes and active lesions in the heart, aorta, testes, pancreas and liver. Biologic implantation tests have indicated that the spirochete, though dormant in the body of a carrier, may retain

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<sup>1</sup> Stokes, J. H., Cole, H. N., Moore, J. E., O'Leary, P. A., Parran, T., Jr., and Wile, U. J. Cutaneous and Mucosal Relapse in Early Syphilis and Its Differentiation from Reinfection, *Ven. Dis. Inform.* **12**: 55, 1931.

<sup>2</sup> Warthin, A. S. The Persistence of Active Lesions and Spirochetes in the Tissues of Clinically Inactive or "Cured" Syphilis, *Am. J. M. Sc.* **152**: 508, 1916.

its virulence and infectivity indefinitely. According to Warthin latent syphilis is more prevalent than is ordinarily suspected. He stated that the usual estimate, of from 10 to 15 per cent, is too low for the general incidence of syphilis and that 30 per cent expresses a more accurate indication of its prevalence. Warthin claimed that he never saw at postmortem examination a "cured" syphilitic patient. He described such patients as "damaged goods" and expressed the opinion that the damage is progressive. For proof of the eradication of the spirochete it is necessary to present a convincing series of careful necropsy studies on patients known to have had syphilis which was thoroughly treated. Thus far there has been no such proof. On the basis of clinical experience Fournier's dictum, "syphilis slumbers but does not become extinguished," still seems true.

Certain modern concepts of syphilitic infection may help to dispel some of the complacency which has settled around this question. It is now realized that syphilis is a chronic infection in which the invasion by spirochetes becomes generalized early (long before the chancre appears) and that the infection runs a prolonged and varied course, with a tendency to relapse. Individual variations occur according to the constitutional reaction of the patient to the invader. As Schindler<sup>3</sup> has aptly stated, success of treatment depends not on the serologic reaction, nor on a fixed scheme of treatment, but rather on the response of the constitution in the individual patient. There are constitutional differences in morphologic characteristics, function and even immunity which induce variations in response to the spirochete and to the treatment. A suggestive investigation in this direction was made by Nishiwara,<sup>4</sup> who expressed the opinion that there may be a relation between blood grouping and predisposition to disease. He found that the Wassermann reaction became negative with treatment in a higher percentage of patients whose blood belonged to group O or A than in those with blood of group B or A B. The physician who is aware of the importance of constitution as a factor in syphilis will treat the patient, not the spirochete or the serologic reaction. In patients with latent syphilis the serologic reaction may remain positive in spite of maximal treatment. In other patients the reaction becomes negative promptly but the infection may continue. Chatschaturjan<sup>5</sup> extirpated a lymph node from a syphilitic patient who had received six courses of treatment and

3 Schindler, K. *Die Konstitution als Faktor in der Pathologie und Therapie der Syphilis*, Berlin, S. Karger, 1925.

4 Nishiwara, M. *The Relationship of Curability in Syphilis to Constitutional Serology*, Lues. *Bull. Soc. japon. de syph.* **12**, 2, 1935.

5 Chatschaturjan, G. *Latente Syphilis und Inokulation lymphatischer Drüsen*, *Dermat. Ztschr.* **66**, 315, 1933.

presented no symptoms and had negative serologic reactions. On serototal inoculation of a rabbit with this material, a typical chancre developed. In the state of latency there is a balance between the invasive powers of the parasite and the immune reactions of the body. Bergel<sup>6</sup> concluded that agglutination, degeneration and lysis of the spirochete are induced by a lipolytic ferment from the lymphocytes, which constitute the main cellular defense against the spirochete. He explained the altered reactions in patients with tertiary syphilis by the altered nature of the spirochete after long exposure to the defenses of the body. The external lipid layer of the spirochete has been digested, leaving the inner protein substance exposed. This acts as an antigen which induces the reactions typical of tertiary manifestations. Chesney<sup>7</sup> stated that acquired immunity to syphilis is a state of resistance which evolves comparatively slowly and is not always complete. It is based more on tissue reactions than on blood defenses. It is not the function of any one cell, nor is it attained by any known method of immunization. It evolves only as the result of reactive manifestations, though it may not depend on the persistence of infection for its maintenance. Finally, this symbiosis reaches the stage at which a balance has been attained between the host and the parasite, with mutual immunization, so that the organisms may remain viable for decades in the body of the host without increasing in numbers and yet are able to initiate an inflammatory reaction should conditions favor them. Theobald Smith<sup>8</sup> expressed the belief that the prolonged parasitism of the spirochete and the insidious, comparatively mild reactions induced only after a considerable period indicate that there is little that is foreign to the body in the parasite and that its metabolic activity is closely allied to that of the host. These are the conditions of a perfect symbiosis. This shows how difficult is the problem of chemotherapy, namely, to kill the invader without injuring the host. The syphilitic infection has been effectively treated clinically and experimentally by compounds of arsenic, bismuth, mercury, vanadium, platinum and gold. The term "specific treatment" is a misnomer. The present therapeutic armamentarium is a blunderbuss of nonspecific metal therapy, which occasionally wounds the host as well as the parasite. Arsphenamine does not destroy the spirochete in vitro, but some observers think that in the body an arsenoprotein is formed

<sup>6</sup> Bergel, S. *Die Syphilis im Lichte neuer experimentell-biologischer und immuntherapeutischer Untersuchungen*, Jena, Gustav Fischer, 1925.

<sup>7</sup> Chesney, A. M. Acquired Immunity in Syphilis, *Am J Syph* **14** 289, 1930.

<sup>8</sup> Smith, Theobald. An Attempt to Interpret Present Day Uses of Vaccines, *J A M A* **60** 1591 (May 24) 1913.

which is destructive to the parasite. In patients who are resistant to treatment an arsenic compound may form which is comparatively harmless to the parasite. The incidence of relapse in spite of vigorous therapy, latency and resistance to treatment may be due to one or more of the following factors suggested by Ingraham <sup>9</sup> (1) A few of the parasites acquire tolerance for drugs, (2) the spirochetes are situated where a drug does not reach them, (3) the defensive powers of the host are defective, (4) the spirochete passes through a life cycle in which certain forms are resistant to drugs. A study of the comparative morphology and biology of the spirochete has revealed granular and budding forms. The presence of granular forms among the parasites of the spirochete group tends to indicate that this phenomenon is more than a mere degeneration. These facts have induced Marchand, McDonagh, Levaditi and others to postulate the existence of a complex life cycle for the spirochete. The existence of a granular or spore stage may be sufficient to explain resistance to treatment and a tendency to relapse. The actuality of such a life cycle has not been proved or confirmed.

One must therefore be content for the present to regard the spirochete as the sole cause of all the morbid changes associated with syphilis. When one takes into consideration the early generalization of the infection, the tendency to relapse, the uncertainties of modern "specific" therapy, the existence of latent and anergic infection and the little understood immunology of syphilis, a cautious, conservative and skeptical attitude as to the complete biologic cure of the infection seems justified. It is more accurate to speak of "arrest" than of "cure", at least this attitude might discourage a too prevalent optimism and complacency. It is therefore illogical to set a time limit, such as from three to five years, after which a patient may marry presumably with assurance of safety. From an ideal eugenic standpoint the syphilitic person is undesirable marriage material. Should a syphilitic person marry and have progeny? If the syphilitic person insists on his biologic rights tragedy is always possible, even with all the advantages of the highly developed modern treatment. A perusal of the best texts of modern syphilographers since 1910 indicates a tendency to prolong the duration of treatment and medical supervision of the syphilitic candidate for marriage. They recommend continuous treatment until the disease is clinically and serologically "cured," and then a lifetime of medical supervision. The course of syphilis is unpredictable even by the most skilled physician. Since the physician can at no time assure the patient that his body is free from spirochetes, is it safe at any

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<sup>9</sup> Ingraham, N. R. Jr. The Life History of the *Treponema Pallidum*. *Am J Syph* 16:155 1932.

time to assure the syphilitic man that he may marry without endangering his wife and offspring? At best there may be offered a prospect of a reasonable span of life with a minimum of complications and assurance of arresting the infection if it is properly treated in time. As concerns scientific medicine versus syphilis, the ancient struggle continues, with the hope that more profound studies in the biochemistry of the spirochete and more basic researches in immunology and chemotherapy may some day bring the realization of Ehrlich's *therapia sterilisans magna* for this stubborn infection.



# INCREASED REACTIVITY OF THE SKIN TO STAPHYLOCOCCUS TOXIN IN PATIENTS WITH LUPUS ERYTHEMATOSUS

H HANFORD HOPKINS, M D

AND

EARL L BURKY, M D

BALTIMORE

Since 1906 it has been known that filtrates from broth cultures of certain strains of staphylococcus contain a specific exotoxin<sup>1</sup> On this fact, however, general attention was not focused until 1928,<sup>2</sup> when in Bundaberg, Australia, twelve children died after receiving injections of diphtheria antitoxin, which later was shown to have been contaminated with a toxin producing staphylococcus In 1930 Burky<sup>3</sup> isolated similar staphylococci from various cutaneous lesions, and he, as well as others, has published studies dealing with this toxin<sup>4</sup>

In order to determine the reactivity of the skin to this toxin shown by patients with various types of cutaneous diseases, we have performed intracutaneous tests on ninety-seven patients from the dermatologic dispensary The test dose of toxin (Burky's) was 0.1 cc of a 1:100 dilution, injected intracutaneously in the forearm Reactions were observed forty-eight hours later

The purpose of this paper is to report the unusual reactions of fifteen patients who had either active lupus erythematosus or scars resulting from former lesions of the disease

Our results showed that patients with lupus erythematosus reacted much more frequently and violently than did the control group Of the fifteen patients with lupus erythematosus tested, ten, or 66 per cent,

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From the Dermatological Clinic of the Johns Hopkins Hospital and the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital

1 Kraus, R, and Pribram, E Ueber Staphylokokkentoxin und dessen Antitoxin, Wien klin Wchnschr **19** 493, 1906

2 Burnet, F M The Exotoxin of Staphylococcus Pyogenes Aureus, J Path & Bact **32** 717, 1929

3 Burky, E L Personal communication to the authors

4 Burky, E L Studies on Cultures and Broth Filtrates of Staphylococci, J Immunol **24** 93, 115 and 127, 1933, Studies on Cultures and Broth Filtrates of Staphylococci Antitoxin Content of the Rabbit Serums Immune to Staphylococcus Toxin and Precipitin Reactions of Such Serums, ibid **25** 419, 1933

showed a reaction exceeding a total dimension<sup>5</sup> of 10 cm. Of the control group, consisting of eighty-two patients with various cutaneous diseases, such as verruca, eczema, scabies, dermatitis of various types, furunculosis, urticaria, acne vulgaris, chalazion, pityriasis rosea, ecthyma, impetigo and erythema multiforme, only 25 per cent showed a reaction exceeding 10 cm. It is interesting to note that the presence

*Data on the Results of Tests Made on Patients with Lupus Erythematosus\**

Identification	Type of Lesion	Size of Reaction
Brown skinned Negro girl aged 17	Chronic hypertrophic "butterfly" patch, present 1½ years	Local 15 + 5 cm = 20 cm
White man aged 28	Relapsing lesion in scar, resulting from old "butterfly" patch which had healed under gold therapy	Malaise 13 + 6.5 cm = 19.5 cm 12 + 7 cm = 19 cm Tested twice
White woman aged 30	"Butterfly" patch of 4 years' duration	9.5 + 7 cm = 16.5 cm
White woman aged 39	"Butterfly" patch of 5 years' duration	6 + 4.5 cm = 10.5 cm
White man aged 27	"Butterfly" patch of 11 years' duration	5 + 5 cm = 10 cm
White man aged 53	Recurrence in scar of "butterfly" patch, healed with therapy with a gold compound 4 years prior to testing	Fever, headache and chill 11 + 8 cm = 19 cm
White woman aged 33	History of "butterfly" patch healed by therapy with a gold compound several months prior to testing	3 + 4 cm = 7 cm (retested 4 weeks later, 7 + 4 = 11 cm)
White woman aged 54	"Butterfly" patch and other subacute disseminate lesions, resistant to gold compounds	8 + 5 cm = 13 cm
White woman aged 39	Acute disseminate lesions, with moderate constitutional reaction	10 + 6 cm = 16 cm
White woman aged 39	Acute disseminate lesions, patient moribund at time of testing, diagnosis thought to be pellagra by some observers	7.5 + 1.5 cm = 9 cm
White man aged 36	History of previous lesions, none at time of testing	8.5 + 10.5 cm = 19 cm
White man aged 49	Several plaques about ears of 2 months' duration	7 + 5 cm = 12 cm
White woman aged 47	Chronic plaques limited to scalp	6 + 4 cm = 10 cm
White woman aged 32	Chronic plaques limited to scalp	9 + 6 cm = 15 cm

\* Sixty-six per cent of the patients tested showed a reaction exceeding a total dimension of 10 cm. Only 25 per cent of eighty-two patients in a control group, with various diseases of the skin other than lupus erythematosus, showed a reaction exceeding 10 cm.

of an active lesion of lupus erythematosus was not necessary to provoke a strong reaction, patients with scars reacted just as strongly in some instances. The patient with the least reaction was moribund when tested.

This study indicates that patients with lupus erythematosus as a group react more intensely to staphylococcus toxin than do patients with other common cutaneous diseases. It is possible that the test may be of some aid in the diagnosis of questionable cases of the disease.

<sup>5</sup> The dimension is obtained by adding the length and breadth of the reaction.

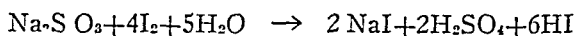
## Minor Notes

### TREATMENT OF IODINE BURNS WITH SODIUM THIOSULFATE SOLUTION

RICHARD L. SUTTON JR., M.D., KANSAS CITY, MO

Tincture of iodine is a commonly used and valuable topical antiseptic, but when applied to some skins it can cause an acute dermatitis, which rapidly becomes vesicular and sometimes even ulcerates. It is well to know that a chemical antidote is readily available and strikingly effective.

Sodium thiosulfate in a weak aqueous solution is harmless and soothing as a wet dressing. It reacts with iodine in this fashion:



A patient, Mrs. W., aged 42, underwent an operative procedure wherein radium was inserted into the uterine cavity to inhibit abnormal bleeding. The usual surgical preparation included painting the external genitalia, the thighs and the buttocks with tincture of iodine. As soon as the patient recovered from the effects of the anesthetic, she complained of burning of these areas and informed her surgeon that on previous occasions severe reactions had followed the application of iodine to her skin. Although the excess amount of iodine had been removed with alcohol at the time of the operation and further effort was made at once to remove what remained, the irritation progressed and vesiculation occurred within twenty-four hours in spite of the application of zinc oxide ointment. At that time the severe dermatitis, which was limited sharply to the area where the iodine was applied, consisted of large and multilocular vesicles, containing clear yellow fluid, in confluent patches. A solution of sodium thiosulfate, 1 200 (one drachm [36 Gm.] to a quart of water [946 cc.]) was applied as a wet pack. This was comforting to the patient and was spectacular in relieving the inflammation. No new vesicles appeared, and in two more days the skin looked healthy and dry and was peeling as after a violent sunburn. The patient was certain that this was the quickest healing in her experience with iodine burns, for she had had them before.

A solution of sodium thiosulfate (1 200) applied on a cotton pad to my own skin on which tincture of iodine had been swabbed and allowed to dry removed all visible trace of discoloration from the iodine after six minutes. If to a few drops of tincture of iodine is added a sufficient amount of solution of sodium thiosulfate, the mixture instantly becomes clear, colorless and transparent. The blue stain on cloth produced by a combination of starch and iodine is similarly decolorized. A solution of sodium thiosulfate (1 200) is safe for wet dressings. I have used it frequently in the treatment of tinea and have never seen any harmful effects.

I thought for a time that this therapeutic idea was original with me, but Dr. L. A. Calkins tells me that he has known it for some time and that a student of his had the same inspiration several years ago. Webster<sup>1</sup> in his "Toxicology" suggests gastric lavage with a 5 per cent solution of sodium thiosulfate as an alternative to the use of starchy fluids in the treatment of poisoning by iodine taken by mouth.

Wet packs of sodium thiosulfate constitute specific treatment for iodine burns.

1308 Bryant Building

<sup>1</sup> Webster, R. W. Toxicology, Philadelphia, W. B. Saunders Company, 1930, p. 387.

# Obituary

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JOSEF JADASSOHN

1863-1936

On March 24, 1936, dermatology sustained an irreparable loss through the death of Geheimrat Josef Jadassohn, emeritus professor of dermatology and syphilology of the University of Breslau. He died suddenly in Zurich, Switzerland, after an operation for acute abdominal obstruction.

Jadassohn was born in the small town of Liegnitz, Germany. He pursued his medical studies in the universities of Göttingen, Heidelberg and Breslau, receiving his degree in 1888.

From 1887 to 1892, he was the assistant to Albert Neisser in the dermatologic clinic of the University of Breslau. During these years a firm and lasting friendship was established between Neisser and Jadassohn, and they collaborated on many significant contributions in the fields of syphilis, gonorrhea, tuberculosis of the skin and atrophy of the skin and in the histopathologic investigations of cutaneous diseases.

In 1892, Jadassohn was appointed chief of the dermatologic division of the Allerheiligen Hospital in Breslau. Here he remained until 1896, and during these four years he contributed numerous valuable studies. Jadassohn's early contributions clearly showed a definite trend toward certain special problems of basic biologic significance, which later became the pattern of his life's medical work. His astounding knowledge of almost every aspect of medicine and biology, combined with his extraordinary breadth of vision, enabled him to exert great influence in bringing dermatology back into the domain of medicine. Jadassohn's subjects of investigation included such diverse interests as the genesis of eczema, the morphology and immunology of tuberculosis of the skin, of tuberculids and of the dermatomycoses, the histology and genesis of congenital anomalies, gonorrhea, chancroid, and all forms of research in syphilis, as well as sociologic studies in the prevention of venereal disease, notably the legal regulation of prostitution.

The quality of this early work gained merited recognition, and in 1896, when only 33 years old, Jadassohn was called to the chair of dermatology at the University of Bern, Switzerland. He occupied this position until 1917, and it was during these years that he attained the stature of an international authority on almost every aspect of dermatology and venereology.

During these undisturbed and happy years in Bern, Jadassohn's accomplishments were prodigious. Today, many seemingly isolated and daring outposts of ultramodern dermatology are merely consolidating the advance made by the pioneer work of Jadassohn and his school. While in Bern, the sphere of Jadassohn's influence widened, not only because of his own work and that of his assistants and pupils but also because of his inspiration and guidance of illustrious disciples among them Bruno Bloch and Lewandowsky.

In 1917 Jadassohn was called to Breslau to succeed Neisser. And in Breslau, with its richer material, superior equipment and large personnel, Jadassohn was able to increase the scope of his work and vastly to widen the sphere of his influence. His vitality and interests never slackened, and his achievements continued to surpass themselves to the last days of his life, long after he had been retired from the chair in Breslau (1931) after two special prolongations beyond the usual age limit. In Breslau, as in Bern, Jadassohn's teaching and example led to the development of distinguished disciples, such as M. Jessner, Mautenstein, Biberstein, W. Frei, R. L. Mayer, St. Epstein, Lenhoff, Kogoj, Jordan, Truffi, Bizozzero, Dohi, H. N. Cole, Zwick, W. Freudenthal and Werner Jadassohn.

The published work of Josef Jadassohn is so voluminous and the subjects cover such wide and varied fields that the student can scarcely "read up" on any subject in dermatology and venereology without encountering some fundamental contribution from Jadassohn's pen.

It is obviously impossible to enumerate the achievements of this man of unique accomplishments and untiring zeal, nor is it possible to select, other than arbitrarily, certain contributions as being more worthy of mention than many others of equally preeminent value. It can never be forgotten that Jadassohn was the first dermatologist to apply objective experimental methods to the study of the immunology of the skin; the first to study cutaneous reactions and to apply a patch test; the first to study the precise influences of idiosyncrasy and allergy in the production of eczema, of drug eruptions, of tuberculids and of trichophytids, and the first fully to recognize the influence of immunobiologic effects on the morphology and course of many other dermatoses.

He elaborated many refinements in the modern diagnosis of gonorrhea and urged the general use of complement-fixation tests and of culture methods in the more accurate diagnosis of this disease.

And it is most likely that the employment of arsphenamine in the treatment of syphilis would not have survived the early accidents and the onslaughts of its opponents had not Neisser and Jadassohn stoutly and passionately championed the continued use of Ehrlich's drug in the face of the most bitter and often acrimonious opposition.

Jadassohn was considered by many to be the greatest authority of his time on such varied and diverse conditions as tuberculosis of the skin, the pyodermas, pellagra, the nevi, the dermatomycoses, drug eruptions and eczema, and his many works on these subjects have brought forth both clarity and new approaches.

Although he had never been in the tropics, he was a world-wide acknowledged authority on leprosy, and it is noteworthy that he was recently asked by the Brazilian government to inaugurate and to direct, as well as to organize, the research at the new Institute for the Study of Leprosy.

Jadassohn was the almost poetical creator of the majority of the dynamic problems of modern dermatologic research. The immunologic concepts of Jadassohn and Lewandowsky's law, of positive anergy and of localized sensitization and immunization are all his, and so also are the present classifications of the pyodermas, of the drug eruptions and of the tuberculodermas.

His incredible faculties of clinical and histologic observation and description are evidenced by the many sharply portrayed disease entities which bear his name, such as Jadassohn's blue nevus, Jadassohn's anetoderma, Jadassohn's granulosus rubra nasi, Jadassohn's psammoma, Jadassohn's dermatitis psoriasiformis et lichenoides and Jadassohn's lichen trichophyticus (lichenoid trichophytid).

In addition to possessing all these qualities of the scientist, Jadassohn was preeminently a physician, a truly remarkable diagnostician and therapist.

Jadassohn was not only the most eminent dermatologist but the recognized foremost venereologist of his time, and as such he was called on by the League of Nations to serve as the judge of serologic methods at the first international competition of serologists in Montevideo. He was a member of the Hygienic Commission of the League of Nations and chairman of the committees on the treatment of syphilis and on venereal diseases, he was also the president of the German Society for Combating Venereal Disease. Moreover, the German government officially called on Jadassohn to formulate the law for the control of venereal diseases which came into effect in 1927.

Besides holding innumerable other positions of responsibility and honor, Jadassohn was a director and perpetual general secretary of the German Dermatologic Society. He was editor of the *Archiv für Dermatologie und Syphilis* and co-editor of the *Zentralblatt für Haut- und Geschlechtskrankheiten* and fellow of innumerable dermatologic and corresponding member and fellow of the *Deutsche Dermatologische Wochenschrift* and of the *Klinische Wochenschrift*. He was honorary and other medical societies, including the American Dermatologic Association and the New York Academy of Medicine.

No mention of Jadassohn's achievements can omit the "Handbuch der Haut- und Geschlechtskrankheiten" This encyclopedic work—forty-one volumes—will stand as a monument to Jadassohn's labors as its guiding spirit and editor in chief He also contributed several invaluable chapters

Jadassohn the man, the personality, was as distinguished as Jadassohn the scientist His integrity, his kindness, his indescribable charm, his delightful sense of humor and his genuine modesty—his character, in short—was a rare addition to his intellectual gifts

He himself said that in his younger days he was given to outbursts of temper and was inclined to be intolerant toward those who did not, in his opinion, apply the proper standards of industry and scrupulousness to the work at hand No traces of this choleric disposition remained noticeable during his later years It was unique and profoundly touching to observe the adoration which Jadassohn's assistants felt for the "chief"

To epitomize the essential quality of this man's greatness, one can do no better than quote his son, who said "My father is the personification of the sense of duty" And, in truth, duty was the motif of Josef Jadassohn's life duty to his fellow man, duty to his craft and duty to his family Humanity has lost a noble man, and dermatology, its greatest leader

M B S

#### AN APPRECIATION

On a hot day in August 1911, while approaching the dermatology building of the old Inselspital at Bern, Switzerland, I ran into a somewhat short, stout man with mussed black hair and a very pleasing face I asked him, in a halting German, where might I get in touch with the Herrn Professor Doktor J Jadassohn He immediately took me by the hand, in a kindly, fatherly way, and asked me who I was and for what I was desirous of seeing him, as he was Professor Jadassohn That was my introduction to one of the finest, most lovable and kindest men that it has ever been my experience to meet

No one was idle in his clinic Within a day or so he had submitted several problems to me, asking me to take my pick I was given a stand in a well lighted passageway, for the old Inselspital did not boast of any elaborate group of buildings They believed rather in specializing in brains, and the university could boast of the following galaxy—Sahli, in internal medicine, Kocher in surgery, Langhans and Wegelin, in pathology, Kronecker, in physiology, Jadassohn, in dermatology, Kolle, in bacteriology and others almost equally famous I was furnished simply with a stool and a plain board stand for my microscope and sections, and I was told that I might go to work Twice a day the staff made rounds in the hospital with the "chief" discussions being

held over patients and over conditions in which he was interested. While Jadassohn believed firmly in properly controlled experimental medicine, with human beings as well as with animals, he was one of the kindest of persons. Many times I have heard him recommend to the chief of staff that certain persons be given an extra portion of bread and milk. There were several physicians outside his regular staff studying at the clinic. Included among them were two men from Japan, one from Russia, a woman physician from Stockholm, several Germans and another American besides myself. Time was never wasted in Jadassohn's clinic. The example furnished to all the assistants and to the outsiders by the "chief" was in itself sufficient. His delight was in a problem. He worked day in and day out. It was common knowledge in the clinic that when he took a vacation, which was always a short one, somewhere in the Swiss mountains or on a Swiss lake, he would take along a batch of papers, two or three boxes of slides and his microscope. He seemed to be interested in nothing except his beloved dermatology and the various problems connected with it.

At that period he had become especially interested in the various phases of immunology in relation to dermatophytosis and to tuberculosis—studies that, as time went on, were to make him world famous. It seemed to be his whole life.

One day his wife explained to me that they had some tickets for the Stadt Orchestra and that since Professor Jadassohn was not especially interested in music, though his brother had been the great pianist and composer, Jadassohn, she would be happy if I would accept one of the tickets, and thereafter it was my especial pleasure throughout the winter to have one of his tickets for the Stadt Orchestra. The professor preferred to stay at home and work on some of his numerous problems.

While I have stated that he was always kindly, always interested in the various studies, he could be critical of results, and he was never satisfied until they actually crystallized into something very tangible. He had no time for a slacker. He would accept no short cut, and he did not believe in rushing into print. When my first paper was completed and I made the comment that I regretted very much handing in an untyped paper, I was told that if I cared to come to his home I might use his typewriter for that purpose, such little courtesies as this were shown to all in the clinic. No man who has ever worked with Jadassohn can have any but the kindest recollections of this great man and scientist.

He never spoke ill of any one. Tension was rather high when I was in the clinic at the time of the Agadir episode, and although Jadassohn was a German I never heard him speak in any but the highest



words of admiration of the French school of dermatology. He was particularly an admirer of Brocq, of Darier and of Sabouraud.

Jadassohn furnishes an example for all the dermatologic world of a man interested in truth and in a medical science that has no bounds of race, color or creed. He was one of the great men of his time. As a teacher and investigator, he was unsurpassed, and men proud to acknowledge him as teacher are spread over the entire world.

H N C

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A number of American colleagues, who were charmed by Jadassohn's personality on the occasion of his visit to the United States, expressed the opinion that the guest of the American Dermatological Association was displaying, if I may so put it, his "company manners." This opinion came to me as a surprise, because Jadassohn's conduct in America differed in no way from his unaffected, engaging simplicity of bearing as I observed it during a period of nearly ten years in the Dermatologische Universitäts-Klinik in Bern, Switzerland, where I received my fundamental instructions from the *praeceptor mundi in rebus dermatologicis*. At no time did Jadassohn "live on high in frigid dignity," on the contrary, he taught by his daily example the principle of conduct which he professed and which one finds embodied in Goethe's imperative

"Edel sei der Mensch,  
Hilfreich und gut!"

It was in this spirit that Jadassohn gave to the assistants and to the research men in his clinic so freely of his time, from the day of their arrival, when he advised them how to find living quarters, until the time of their departure, when he provided them with letters of introduction to other clinics and celebrities.

In assigning research problems, he sought to discover the particular interests and specific qualifications of the student, he pointed out the terra incognita which the investigation was intended to explore, he assisted the search in the literature with references and reprints from his extensive private library. In making the rounds of wards and in discussing cases, Jadassohn developed the essential characteristics with the ease and clearness which are the enviable attributes of a great teacher. The skill and simplicity with which he interpreted the signs and symptoms of a disease in terms of a dynamic pathology are unforgettable. He instilled in his students a deep interest in unusual and rare conditions because as he declared, they so frequently lead to discoveries. What he taught us will remain in our memory.

As a man, Jadassohn was quiet and democratic, with a ready sense of lively humor. But though he was *suavis in modo*, as a critic he was *fortis in re*. His modesty was so great that his publication on Ehlich's aismical was prefaced by the aphorism of the Königsberg philosopher "Wenn die Könige bauen, haben die Karner Arbeit" ("When the kings build, the truckmen have work"). Jadassohn's kindness inspired affection, and his high ideals fostered universal respect in all who came in contact with him.

To all those who have enjoyed the privilege of working with Jadassohn at any period of his life, but perhaps most of all to those who were with him in Bern, as I see it in retrospect the happiest period of Jadassohn's life, his death comes as a reminder of a time when his stimulating interest and enthusiastic desire to help were a part of their own best and busiest days!

The infrangible, enduring bond between Jadassohn and those who worked with him is one of the most remarkable tributes to his character. In the singularly appropriate words of Ruskin "That man is richest who, having perfected the functions of his own life to the utmost, has also the widest helpful influence over the lives of others!"

K G Z

## Correspondence

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### SODIUM THIOSULFATE IN THE TREATMENT OF ARSENIC POISONING

*To the Editor* —In a recent article entitled "Study of a Group of Handlers of Arsenic Tri-Oxide," by H G Irvine and D D Turnacliff (*ARCH DERMAT & SYPH* **33** 306 [Feb] 1936), mention was made that no book on toxicology or industrial medicine, published even as late as 1934, includes mention of the use of sodium thiosulfate for the treatment of industrial arsenic poisoning. This point is well taken, however, in the column of Queries and Minor Notes in *The Journal of the American Medical Association* (**99** 1374 [Oct 15] 1932), the use of this drug was advised in a series of cases of dermatoses in laborers who sprayed potato plants with a combination of calcium arsenite and paris green. This reference was used in my recent paper entitled "Industrial Dermatoses Treatment and Legal Aspects. Review of Recent Literature," published in the *Journal of Industrial Hygiene* (**17** 138 [July] 1935).

JOHN GODWIN DOWNING, M D Boston

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

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SPINDLE-CELL EPIDERMOID CARCINOMA HAYES E MARTIN and FRED W STEWART, Am J Cancer **24** 273 (June) 1935

The authors describe a malignant metastasizing epidermoid carcinoma of the skin and mucosa. Eight cases are reported, most of which occurred in, or adjacent to, the lip. The lesions resembled carcinoma clinically and exhibited sarcomatous features histologically. Etiologic consideration is given particularly to roentgen and also to radium irradiation, cautery, wounds and other traumas resulting in inflammatory cutaneous changes in fibrous tissue. Cautery or endothermy applied to tissue exhibiting scars due to radiation is credited for the development of spindle cell carcinomas. These lesions are not radiosensitive and require wide and deep excision.

THE MALIGNANT TUMORS OF THE PERIPHERAL NERVES ARTHUR P STOUT, Am J Cancer **25** 1 (Sept) 1935

The most common primary malignant tumors of the peripheral nerves are fibrosarcomas, the majority of these occur in patients with Recklinghausen's disease and apparently originate in preexisting neurofibromatous nodules. Surgical removal is frequently followed by recurrences, and in 20 per cent of the cases metastasis occurs. These lesions are very radioresistant. Less frequent, and likewise of mesoblastic origin, are neurofibromas. Malignant tumors of peripheral nerves of epithelial origin are rare. Stout disputes Ewing's contention that the majority of spindle cell sarcomas of the skin are of neurogenic origin.

ON THE DYSONTOGENETIC ORIGIN OF BASAL-CELL CARCINOMA JOSEPH MCFARLAND, EMMETT CICCONE and JOSEPH GELEHRTER, Am J Cancer **25** 273 (Oct) 1935

A review of the recorded localizations of basal cell carcinomas in two separate groups of hospitalized patients and a comparison of these observations with those of Glasunow indicated an anatomic distribution similar to that of sequestration dermoids and mixed tumors and a conformity with the localization of embryonic facial fissures. The authors therefore conclude that basal cell carcinomas may be dysontogenetic tumors which originate in imperfections in the closure of the embryonal facial fissures.

THE DIFFERENTIAL MORTALITY FROM CANCER IN THE WHITE AND COLORED POPULATION S J HOLMES, Am J Cancer **25** 358 (Oct) 1935

Holmes states that racial differences apparently account for marked variations between the death rate from cancer in white patients and that in Negro patients. The younger age groups showed higher mortality among Negroes than among white patients, and the higher age groups showed the opposite. Among patients with cancer of the skin and buccal tissues the death rate was much higher for the white race, particularly in the age group beyond 50.

TUMORS OF THE PERIPHERAL NERVES CHARLES F GESCHICKTER, Am J Cancer **25** 377 (Oct) 1935

This paper includes a study of forty cases of Recklinghausen's disease. The tumors observed in cases of Recklinghausen's disease are usually undifferentiated.

benign lesions of the nerve sheath that may recur after removal and that may undergo malignant change. They usually consist of reticulated myxomatous tissue and have been referred to as fibromyxomas, fibroneuromas and myxoid neurinomas. The malignant lesions are usually sarcomas of the nerve sheath. Recklinghausen's disease is a congenital disturbance of the nerve sheaths resulting in the formation of multiple subepidermal nodules along the distribution of the peripheral nerves, tumors of deeper nerve trunks and roots and disturbances in pigmentation. It may be complicated by meningeal tumors, angiomas, lipomas, plexiform neuromas, spina bifida and localized hypertrophy of a limb. Fifteen of the forty cases studied terminated fatally because of the occurrence of sarcomatous and other tumors.

THE RELATIONSHIP BETWEEN VASCULARITY AND THE REACTION TO RADIUM OF  
SQUAMOUS EPITHELIUM. M. G. SEELIG, C. T. ECKERT and Z. K. COOPER,  
Am J Cancer **25** 585 (Nov) 1935

On the basis of experiments on rabbit ears the investigators concluded that changes in the vascularity of the skin do not alter its radiosensitivity and that the latter is an inherent quality of the cell, variable in different subjects.

A CASE OF SCHULLER-CHRISTIAN'S DISEASE UNDER OBSERVATION FOR NINE YEARS  
W. A. HANSON, L. H. FOWLER and E. T. BELL, Am J Cancer **25** 768 (Dec)  
1935

The authors state that Schuller-Christian's disease is a form of xanthomatosis in which the xanthomas develop in various organs, especially in the bones of the skull. In the case reported there was involvement of the flat bones of the skull, the lumbar portion of the spine, the ilia and lymph nodes. Cutaneous lesions were not reported.

FOERSTER, Milwaukee

CONGENITAL SYPHILIS IN CHILDREN. F. R. SMITH, Am J Syph & Neurol  
**19** 532 (Oct) 1935

The material for this paper was obtained from the records of 991 children with congenital syphilis seen in the Harriet Lane Home for Invalid Children, the pediatric department of the Johns Hopkins Hospital, from the opening, in 1914, to June 30, 1934.

The results of treatment in 279 patients with early congenital syphilis were analyzed. These patients were under surveillance for a minimal period of two, and a mean period of six and two-tenths, years. Congenital syphilis is a material factor in the cause of death in children under 6 months of age, the number of deaths due to the disease decreasing rapidly after that age. The beneficial results of prenatal treatment on the child are in direct proportion to the amount of treatment given the mother. "Ultimate satisfactory clinical response" to treatment is in direct proportion to the age at which treatment is started and to the amount of treatment. The incidence of Wassermann-fastness increases as the start of treatment is delayed. Its presence increases the danger of relapse and progression. Inadequate treatment does not delay the time of the appearance of lesions indicating a relapse, but adequate treatment prevents them.

All forms of early congenital syphilis are readily amenable to modern methods of treatment with the exception of clinical neurosyphilis.

THE DIAGNOSIS OF INFANTILE CONGENITAL SYPHILIS DURING THE PERIOD OF  
DOUBT. N. R. INGRAHAM JR, Am J Syph & Neurol **19** 547 (Oct) 1935

Infants born of mothers with latent or partially treated syphilis are apparently healthy at the time of birth in such a large percentage of cases that it is difficult or impossible to recognize early congenital syphilis, when it is present, by ordinary routine examination. About one half of such children are infected.

It is essential to give the new-born infant of a syphilitic mother the benefit of special study.

# ABSTRACTS FROM CURRENT LITERATURE

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As regards children of mothers with latent or partially treated syphilis, physical examination of the child at the time of birth is of diagnostic value in not more than from 2 to 3 per cent of the cases, serologic tests of the blood are of some diagnostic worth in about 15 per cent, but of absolute diagnostic value in only about 1 or 2 per cent, of the cases. Dark-field examination of the umbilical vein, will, in routine practice, reveal spirochetes in about 20 per cent of infants born of syphilitic mothers while roentgen examination of the long bones will show an osteochondritis in about 30 per cent of such infants at the time of birth. A combination of all these methods of study will detect in the first week of life at least half, and by the end of the second month about three fourths, of the babies ultimately proved to be syphilitic. There is, then, in the period of doubt, no absolutely reliable method of diagnosis as do exist make it possible to detect the application of such diagnostic methods and keep the mortality and infantile congenital syphilis while it is yet "curable" and keep the mortality and morbidity rate among the syphilitic infants at low figures. It seems rational that an infant suspected of having contracted syphilis in utero from his mother should not be treated for this disease until he has been proved to have it and that he should not be subjected to antisyphilitic treatment merely because there is danger of his having the disease.

REUTER, Milwaukee

**SYPHILIS** A REVIEW OF THE RECENT LITERATURE JOSEPH E MOORE, Arch Int Med 56 1015 (Nov ) 1935

Moore gives abstracts of articles published in 1934 and up to July 1935, some of these have been abstracted and others have been published in earlier issues of ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY

JAMIESON, Detroit

**SYPHILITIC AORTITIS IN CHILDHOOD AND YOUTH** REPORT OF TWO CASES WITH SUDDEN DEATH ROBERT F NORRIS, Bull Johns Hopkins Hosp 57 206 (Oct ) 1935

Norris reports 2 cases of syphilitic aortitis. One occurred in a 9 year old Negro girl and the other in a white boy aged 17. There was considerable evidence that the lesions were of congenital origin. The patients were the only ones among 14,000 patients examined at autopsy at the Johns Hopkins Hospital who showed pathologic changes suggestive of congenital syphilis of the aorta. In each case death was comparatively sudden.

NELSON PAUL ANDERSON, Los Angeles

**THE ADRENAL PROBLEM** FRANK A HARTMAN, Endocrinology 19 633 (Nov -Dec ) 1935

In a review of recent work on the adrenal glands Hartman points out that in experimental chronic adrenal insufficiency produced by the administration of inadequate doses of adrenal cortex extract in adrenalectomized animals pigmentation has been observed only in monkeys. The absence of pigmentation in other animals is of interest because hyperpigmentation is such a striking feature of Addison's disease.

LYNCH, St Paul

**THE INTRADERMAL REACTION FOR CHANCROIDS WITH CHANCROIDAL BUBO PUS** H N COLE and E A LEVIN, J A M A 105 2040 (Dec 21) 1935

Cole and Levin confirm the observations of previous workers as to the specificity of an antigen prepared from the pus of chancroidal buboes and used as an intradermal diagnostic test for chancroid. The antigen is prepared from a chancroidal bubo which has been proved to be chancroidal by the presence of Ducrey's bacillus either in the primary lesion or in pus from the bubo. The patient from whom the material is obtained for the test is required to have a negative Frei reaction and the antigen prepared must not produce reactions in

patients with lymphogranuloma inguinale. Negative reactions to the intracutaneous test were noted in patients with lymphogranuloma inguinale, gonorrhea, granuloma inguinale and pulmonary tuberculosis, in patients with early and with late stages of syphilis, in pregnant women, in patients with various cutaneous diseases, including mycotic infections, and in patients with varied conditions who were in wards of the medical service. Of fifty-two patients who had positive reactions to the intradermal test, five had no evidence of active infection or history of such an infection, twenty-two harbored the organism, five were known to have had a previous infection, and twenty had a history of previous venereal ulceration and suppurating buboes. There was an average latent period of five weeks from the presence of the ulceration to the production of a positive reaction. The presence of a chancroidal bubo seemed to increase the rapidity and intensity of the reaction to the intracutaneous test. Positive and negative reactions noted from the injection of the pus antigen used in the investigation closely paralleled those obtained with a stabilized streptococcus vaccine, the latter gave a more clearcut and stronger reaction. The authors conclude that the allergic response to the intracutaneous test in a patient with a chancroidal infection persists for at least from thirty to thirty-four years and probably for life. The therapeutic results obtained by subcutaneous injection of the material were good in several instances of resistant infection.

CAUSAL THERAPY OF CONTACT DERMATITIS THEODORE CORNBLEET, J. A. M. A.  
105 2062 (Dec 21) 1935

Cornbleet mentions that in establishing the diagnosis of contact dermatitis it is important to note the distribution and morphology of the lesions in order to detect the agent responsible for the dermatitis. It is necessary to obtain thorough information as to the patient's work, activities and environment. It is also helpful to have some knowledge of the common irritants and allergins to which the patient might be exposed, as well as of the agents capable of producing the greatest number of sensitivities. All materials which are suspected should be applied as patch tests, suitable concentrations being used, to the normal skin of the patient. The interpretation of the results of the test requires experience, and attention is drawn to false negative and false positive reactions. The final conclusion as to the cause of the dermatitis is the demonstration of clinical cure when a suspected allergin is removed from the patient's environment. Desensitization is occasionally successful, and in some cases a cure may be effected by merely preventing contact between the offending allergin and the patient.

RADIOTHERAPY (ROENTGEN RAYS, RADIUM) ARTHUR U. DESJARDINS, J. A.  
M. A. 105 2064 (Dec 21), 2153 (Dec 28) 1935

Among inflammatory conditions notably amenable to roentgen therapy may be mentioned furuncle, carbuncle, acute simple adenitis, acute parotitis, abscess and cellulitis of soft tissues, onychia and paronychia, mastitis, sinusitis, mastoiditis and delayed resolution of lobar pneumonia.

The main factor in the action of the rays in these acute inflammatory conditions consists in the destruction of the infiltrating leukocytes. It seems likely that the destruction of the leukocytes liberates the antibodies and other protecting substances previously elaborated within the cells and thus makes these substances more readily available for defensive purposes than when they were in the intact cells. Chronic inflammations such as tuberculous adenitis and peritonitis, actinomycosis and blastomycosis are also amenable to roentgen therapy. The mode of action in the latter disease depends on the degree of leukocytic infiltration and also on the proportion of connective tissue and of degenerative material and calcium.

Desjardins classifies tumors according to the degree of their radiosensitivity. The first class embraces radiosensitive tumors, the second class, moderately radio-

sensitive tumors, and the third class includes radioresistant tumors. Basal cell epithelioma is considered to belong in the first class, whereas prickle cell epithelioma is placed in the second class. Melanomas are the most resistant of neoplasms.

Each variety of cell in the body is specifically sensitive to roentgen rays or to radium. According to Desjardins, cells may be classified in the order of their degree of sensitiveness as follows: (1) lymphoid cells, (2) polymorphonuclear leukocytes and eosinophils in the blood or tissues, (3) epithelial cells, (4) endothelial cells, (5) connective tissue cells, (6) muscle cells, (7) bone cells, (8) fat cells, (9) nerve cells. The skin may tolerate with impunity a considerable amount of roentgen rays, but when the limited tolerance is exceeded a series of reactive changes occur. Roentgen ray dermatitis is manifested by early and late effects. The mucous membranes are of approximately the same sensitivity as the skin. Desjardins does not believe that there is any stimulating effect from roentgen or radium radiation. Stimulating effects apparently resulting from exposure to small doses of roentgen rays indicate exceptional radiosensitivity. In the treatment of inflammatory disease by means of roentgen and radium radiation, small or moderate doses only are employed. The more acute the lesion, the smaller is the dose of rays required. If the treatment is given early during the stage of leukocytic infiltration and before suppuration has set in, the results are apt to be better than if given later. Pain is frequently relieved by radiation.

ARTIFICIAL FEVER THERAPY OF SYPHILIS WALTER M. SIMPSON, J. A. M. A.  
105 2132 (Dec 28) 1935

Simpson treated 175 patients with syphilis by means of artificial fever therapy. The apparatus used is known as the Kettering hypertherm and consists of an insulated cabinet in which the nude patient lies on an air mattress. The interior is air conditioned, the temperature being regulated by a thermostat. The humidity is also kept constant, which adds to the safety and comfort of the patient. High frequency currents are not used. Simpson agrees with other observers as to the value of artificial fever therapy in the management of neurosyphilis. His results compare favorably with those obtained by the use of malarial therapy. The advantages of artificial fever therapy over malarial therapy are that the former does not require hospitalization, is less time consuming and involves less hazard to the patient. Patients with primary or early secondary syphilis also received artificial fever therapy, and the improvement obtained leads Simpson to state that this method may be a useful adjunct to chemotherapy in the treatment of early syphilis. He expresses the belief that artificial fever therapy fortifies and intensifies the action of antisyphilitic chemotherapeutic agents.

INGUINAL GLAND METASTASES IN CARCINOMA OF THE PENIS BENJAMIN S.  
BARRINGER, J. A. M. A. 106 21 (Jan 4) 1936

Barringer reported on 100 cases of carcinoma of the penis which he abstracted and correlated from the records of the Memorial Hospital for the Treatment of Cancer and Allied Diseases in New York. In 63 cases only the primary lesion developed. In 37, or a little more than one third of the patients, metastases to the groin occurred. Nine of these 37 patients were still living at the time the report was made, the remaining 28 died of carcinoma and 1 of these lived more than three years after the initial observation. One half of those who died did so in the first year. From his study, Barringer concluded that inguinal metastases are exceedingly difficult to cure. He suggests that the primary lesion should be surgically removed as the first step in treatment. Removal of material for biopsy by aspiration of the inguinal nodes is imperative, and if cancer is present a combination of external irradiation and implantation of radon seeds through an incision and under vision seem to offer the best outlook.



**LUPUS CARCINOMA** REPORT OF AN UNUSUAL CASE OF CARCINOMA FOLLOWING INJURY AND IMPLANTED LUPUS VULGARIS ON THE LEFT UPPER EXTREMITY  
HERMAN GOODMAN, J Indust Hyg **17** 276 (Nov) 1935

Goodman describes a case of lupus vulgaris of the left elbow immediately following a minor occupational trauma, neoplastic changes revealed by microscopic examination took place within six months of the time of occurrence of the trauma. After excision and skin graft the lesions of lupus recurred. Goodman suggests that the tuberculous process developed as a result of the fact that the patient's wound was dressed with the soiled handkerchief of a fellow worker.

WIEDER, Milwaukee

**FUNGUS DISEASES OF THE SKIN** ARTHUR M GREENWOOD, New England J Med **213** 363 (Aug 22) 1935

Laboratory examinations are the final resort in the diagnosis of diseases due to fungi. The procedure for examination of epidermal scales is simple but time consuming. According to Greenwood, the "mosaic" fungus is not a fungus. Biologic investigations along the lines of sensitization and allergic reactions are briefly discussed. Exacerbation of a chronic fungous infection of the skin by industrial conditions and fungous infections superimposed on industrial dermatitis have been held to justify requests for compensation as causes of industrial disability in Massachusetts. A fairly complete but brief discussion of therapy is presented, the highly irritating action of most proprietary remedies is emphasized. The location of the infection should be kept in mind when therapy is instituted. The two fundamental factors are emphasized: (1) the elimination of articles of clothing which encourage the growth of fungi, such as wool socks, heavy boots and gloves, wool underwear and athletic supporters, (2) the avoidance of irritating medication. The acute vesiculopustular reactions are best treated by application of wet dressings during the day, at night ointment containing salicylic acid and sulfur and dusting powder containing boric and tannic acid should be used. The subacute and chronic types are best treated by ointment containing salicylic acid and sulfur, Whitfield's ointment, carbolfuchsin paint or solutions of iodine. Roentgen irradiation produces favorable results, but it must be used with great care. Ethyl iodide should not be used by inexperienced persons nor be employed in unselected cases.

The following factors play a part in reinfection: (1) lack of immunity, (2) ease with which fungi can grow on all fabrics and material used as clothing, (3) ability of fungi to grow on debris and slime which accumulate on various floors, (4) increasing use of gymnasiums and habit of exercising in unsterilizable socks and body clothing, (5) lack of cooperation by authorities in charge of public baths and gymnasiums, (6) incomplete disinfection by standard laundry procedures.

Prophylaxis should include the daily scrubbing of floors with soap powder, the wearing of unlined rubber bathing shoes, the prohibition of walking barefoot, the use of sterilizable cotton garments, and, as the most important factor, the cleanliness of the feet and folds of the body.

APPEL, Boston

**IMPROVEMENT OCCURRING IN CASES OF CALCINOSIS UNIVERSALIS IN CHILDREN**  
F PARKES WEBER, Brit J Dermat **47** 400 (Oct) 1935

The author reports the occurrence of calcinosis universalis in three girls, diminution of the calcareous deposits was shown by roentgen examinations. The treatment included the use of iodides, ketogenic diet and disodium phosphate.

**OCCUPATIONAL ARGYRIA** J M HARKER and DONALD HUNTER, Brit J Dermat **47** 441 (Nov) 1935

The authors report sixteen cases of occupational argyria in seven cases the condition was generalized and in nine it was localized. All the patients in whom

the condition was generalized except one who handled fulminate of silver were employed in the manufacture of silver nitrate. The nine patients with localized argyria were silversmiths.

The generalized argyria occurred in workmen who handled some silver compound, and the eruption resulted from inhalation and ingestion of the silver salt. The localized form occurred in workmen who handled metallic silver, and the eruption was due to accidental tattooing. Generalized argyria is frequently associated with ophthalmologic changes. These consist of a silver staining of the conjunctiva, especially of the inner canthus. The pigment is situated chiefly in Descemet's membrane. To a lesser extent, the same type of ocular pigmentation may occur as the result of the prolonged use of drops containing organic compound of silver. Nine illustrations, five of which are colored, accompany the article.

POST-TRAUMATIC ANGIOMA. F. FOIDMARI, Brit J Dermat **47**:463 (Nov.) 1935

The occurrence of angiomas in a child, 8 years old, following an injury to the nape of the neck is reported. Multiple grouped bluish-red angiomas from the size of a lentil to that of a pea appeared at the injured site in ringlike formation. The skin in the affected area was unchanged. There was no recurrence of the lesions after they were destroyed by electrocoagulation.

Histologic examination showed that the greatest changes occurred in the corium. These consisted in many newly formed capillaries lined with swollen endothelial cells. There was no evidence of inflammation or infiltration.

WIRN, Chicago

THE PRESENCE OF LEISHMANIA DONOVANI IN THE NASAL SECRETION OF CASES OF INDIAN KALA-AZAR. H. E. SHORTT and C. S. SWAMINATH, Indian J M Research **23** 437 (Oct.) 1935

Using ordinary smears of nasal secretion stained by Giemsa's stain, Shortt and Swaminath were able to demonstrate Leishmania Donovanii in two of four cases of Indian kala-azar, thus confirming previous observations of Forkner and Zia.

They advise that in searches for the organism several slides be examined, as some may give negative, and only one may give positive, results.

LEPROSY. A REPORT OF TWENTY-SEVEN CASES TREATED WITH ANTHRAX VACCINE. J. N. ROUSSEL, J Trop Med **38** 133 (June 1) 1935

In treating patients with leprosy Roussel used a vaccine containing attenuated living anthrax bacilli, beginning with 0.125 cc and doubling the dose until a dose of 25 cc was reached. A total of 30 cc was given each patient, the injections being given at intervals of five days.

No change was noted in the lesions until about two or three months after the injections were discontinued. In two thirds of the cases the lesions gradually faded away, the anesthesia being the last symptom to disappear. In the remaining cases a nodular, multiform erythema developed, the leprosy lesions became painful and there was a marked elevation of temperature for three weeks. The nodules and then the leprosy lesions disappeared. The anesthesia also slowly disappeared.

Of the twenty-seven patients treated with the anthrax vaccine, seventeen had maculo-anesthetic leprosy, nine tubercular leprosy and one a mixed type of the disease.

Eighty-eight per cent of the patients with maculo-anesthetic leprosy are apparently well, those with tubercular leprosy were not benefited, the one with the mixed type of the disease is also apparently well.

Emphasis is laid on the statement that the use of this vaccine is urged only for the treatment of maculo-anesthetic leprosy.

Brief reports of five cases are given.

JAMIRSON, Detroit

THE ACTION OF CONCENTRATED SPLENIC EXTRACT IN CASES OF CERTAIN DERMATOSSES (ECZEMA AND URTICARIA) AND OF ASTHMA P VALLERY RADOT and P BLAMOUTIER, Paris med 2 457 (Dec 8) 1934

Among forty-nine patients with eczema treated with splenic extract from which most of the albumin had been removed, twenty-one were cured, in twelve improvement was noted, in eight results were inconclusive and in eight no benefit resulted. Among thirty-five patients with urticaria there were eight complete cures, and in seven improvement or temporary benefit was noted. Among seventeen patients with asthma, four showed improvement, and in two of these there was almost entire relief from asthmatic symptoms.

The authors offer no explanation of their results but restate the theory of Schiff, that the spleen secretes an enzyme which changes trypsinogen into trypsin, and that of Paul, that eczema is caused by a defective metabolism of albumin due to insufficiency of the aforementioned enzyme. Introducing splenic extract into the circulation makes up for this deficiency.

LESLIE, Efanston, III [AM J DIS CHILD]

OBSERVATIONS ON THE SARCOIDS (BESNIER-BOECK'S SYNDROME) AND ON SOME RETICULO-ENDOTHELIAL MANIFESTATIONS OF THE SKIN A CROSTI, Gior ital di dermat e sif 76 975 (Aug) 1935

Crosti calls attention to the fact that in some cases of Besnier-Boeck's syndrome there are hyperplastic granulomatous lesions of pseudoleukemic character which warrant the interpretation given by Schaumann, that the condition is a benign lymphogranulomatosis, and by Pautrier, that it is a systematized reticulohistiocytosis. Three cases are reported to substantiate these views.

CONTRIBUTION TO THE STUDY OF CUTANEOUS SARCOIDS G RADAELI, Gior ital di dermat e sif 76 1000 (Aug) 1935

Radaeli reports a case of lupus pernio of both ears, the disease affecting the auricular canal and the tympanic membrane on one side as well as both auricles. The patient also presented dermo-epidermic nodules on both hands, enlargement of the lymphatic glands and of the tonsils and a tumor of the spleen. The roentgen examination of the chest showed chronic fibrotic tuberculosis. Radaeli concludes that the tuberculous nature of this syndrome has not been sufficiently proved.

THE SARCOID TYPE OF LEPROSY F LISI and F SEBASTIANI, Gior ital di dermat e sif 76 1030 (Aug) 1935

A case of leprosy is reported in which the clinical as well as the histopathologic picture resembled closely that of cutaneous sarcoids. The diagnosis was based on the presence of leprosy bacilli in the lesions.

THE BENGAL ROSE TEST IN CERTAIN DERMATOSES, ESPECIALLY IN CASES OF ECZEMA G ROCCHINI, Gior ital di dermat e sif 76 1076 (Aug) 1935

The study of the hepatic function by means of the bengal rose test was carried out in fifty-seven patients with cutaneous diseases. The conclusions reached by the authors are as follows. In the majority of the cases of occupational eczema of external origin, the hepatic function was normal, in a high percentage of cases of eczema of unknown, presumably of internal origin, the hepatic function was more or less seriously affected. In cases of psoriasis the test gave normal results.

THE ETIOPATHOGENESIS OF ERYTHEMA MULTIFORME IN PORADENITIS INGUINALIS A MIDANA, Gior ital di dermat e sif 76 1091 (Aug) 1935

Midana reports a case of erythema multiforme in a patient suffering from poradenitis inguinalis. The virus was present in the cutaneous lesions. In view

of his observations Midana interprets the cutaneous lesions as the result of an allergic reaction due to localization of the virus in the cutaneous tissues by metastasis

[This interpretation is at variance with the present conception of bacterial allergy in America. Allergic manifestations are regarded as reactions occurring at a distance from the focus of infection, and the offending agent is never recovered from them. Abstractor.]

THE FREI REACTION IN PORADENITIS INGUINALIS LUIGI PERUCCIO, *Gior ital di dermat e sif* 76 1098 (Aug) 1935

Peruccio has observed cases of undoubted poradenitis inguinalis in which the intradermal reaction to the Frei test was negative. He interprets these negative reactions as the result of an anergic condition of the patient or as due possibly to a recent infection in which the defensive mechanism has not reached full development. Further tests are indicated during the course of the disease. [The term "poradenitis inguinalis" has been discarded in America, the name "lymphogranulomatosis inguinalis" is still in use, but there is a tendency to accept the denomination "lymphopathia venerea" proposed by Wise and Sulzberger. Abstractor.]

COMPLEMENT-FIXATION TEST IN PORADENITIS INGUINALIS L. PERUCCIO, *Gior ital di dermat e sif* 76 1101 (Aug) 1935

Complement-fixation tests with antigens prepared from fresh pus in various dilutions gave uniformly negative results in fifteen cases.

CHEILITIS GLANDULARIS AND SIMILAR CONDITIONS JOSE J. PUENTE, *Rev med latino-am* 20 937 (June), 1061 (July) 1935

In this monograph, which covers the subject thoroughly, Puente reports fifty-two cases of cheilitis glandularis. The condition is differentiated from cheilitis glandularis apostematosa of Volkmann, the latter being, according to Puente, a complication developing on the "simplex" type of cheilitis which he describes. Cheilitis glandularis simplex is characterized by enlargement of the orifices of heterotopic salivary glands situated on the lower lip. It is found in about 3 per cent of the patients attending the clinics for patients with cutaneous diseases in Buenos Aires, Argentina, but it occurs mostly among Spaniards residing in the northern part of the country. The condition may remain unknown for a long time, and the patients are, for the most part, entirely unaware of its presence. Several cases of malignant degeneration have been reported in which the epithelial growths seemed to have developed at the expense of the glandular tissue involved. Cheilitis glandularis simplex may be considered as a precancerous condition.

PARDO-CASTILLO, Havana, Cuba

THE MORPHOLOGY OF THE INTERNAL RETICULUM (GOIGI-KOPSCH APPARATUS) OF THE CELLS OF HUMAN SEBACEOUS GLANDS N. MELCZER, *Dermat Ztschr* 71 129 (May) 1935

The Golgi-Kopsch apparatus can be shown in the form of a network by means of special impregnation methods. In the matrix cells of the sebaceous glands this network is seen to be closely set around the nucleus. In the mature cells undergoing necrobiosis the network is scattered through the cytoplasm.

NEW FINDINGS CONCERNING FURUNCLES AND FURUNCULOSIS M. M. LEWIN, *Dermat Ztschr* 71 197 (June) 1935

Lewin obtained cultures of staphylococci from furuncles of patients with a single furuncle and with furunculosis, from apparently normal skin of patients with furunculosis, from patients with weeping dermatoses, and from persons without cutaneous lesions. The virulence of these cultures was determined by intracutaneous

ous injections into the skin of rabbits, the reactions being graded according to their severity and duration. Cultures obtained from the furuncles themselves were most virulent, in a number of instances causing necrotic and pustular reactions. Cultures from normal skin of patients with furunculosis and from areas of weeping dermatoses were somewhat less virulent, and those from patients without cutaneous conditions were only slightly virulent. The author concludes that a virulent strain of staphylococci rather than a reduced resistance is responsible for the development of furuncles.

#### HEAT URTICARIA W. BARTELS, *Dermat Ztschr* **71** 201 (June) 1935

A case of heat urticaria is described in which the wheals were caused by the application of any type of warmth. These outbreaks of urticaria were associated with increase of body temperature as well as with increase of the local temperature. Passive transfer of the sensitivity was unsuccessful. By gradually increasing the applications of heat, desensitization was accomplished.

#### ARE THERE SPECIFIC ANTIBODIES IN THE URINE OF SYPHILITIC PATIENTS? THOMAS PREININGER, *Dermat Ztschr* **72** 10 (Aug) 1935

Preininger reports that he was unable to demonstrate antibodies in the urine of patients with syphilis.

#### SYPHILITIC CHANCRE IN A URETHRA DUPIEX W. KOCH, *Dermat Ztschr* **72** 15 (Aug) 1935

Koch reports the occurrence of a urethral chancre in a patient with a double urethra.

TAUSSIG, San Francisco

#### ERYSIPELAS IN YOUNG CHILDREN E. GORTER, *Maandschr v kindergeneesk* **4** 51 (Nov) 1934

Experience with twenty-six children, of whom only five were 6 years or older, has taught Gorter that it is advisable to treat erysipelas in young children with ultraviolet radiation from a lamp which also sends out short waves. The lamp should have its maximum intensity at the beginning of the radiation, and not only the affected skin but also part of the skin around the eruption should be irradiated. The dose should be about one and one-half times the erythema dose, which must be determined for the sound skin before the beginning of the treatment, as there are great individual variations.

#### A NEW CATAPHORETIC SEROLOGIC REACTION FOR SYPHILIS TESTED ON 1,147 SERUMS L. J. DELBAERE, *Nederl tijdschr v geneesk* **78** 48 (Dec 1) 1934

A serologic reaction is described, based on the lowered electrical charge carried by particles of antigen suspended in the serum of a person with syphilis. The amount of this decrease of charge is measured by means of the cataphoretic rate of displacement of these particles, which is compared with that of a lipid dye that is simultaneously suspended in the serum.

By means of the results obtained with this reaction in tests on 1,147 serums, which were at the same time submitted to the Wassermann test and to two of the usual flocculation tests, it has been proved that this reaction is more sensitive than the very sensitive Muller reaction, and there is no reason to doubt its specificity.

VAN CREVELD, Amsterdam, Netherlands [AM J DIS CHILD]

# Society Transactions

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## CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WILKIN, M.D., *Secretary*

*Regular Meeting, Nov. 20, 1935*

WILLIAM AITKEN PUSEY, M.D., *President, Presiding*

### A CASE FOR DIAGNOSIS Presented by DR. E. P. ZEISLER

This woman, aged 25, has an enlargement of the index finger of the left hand which has been present for fifteen years. Numerous firm subcutaneous nodes can be palpated on the flexor surface, and the tendon sheath is palpable as a firm cord.

Histologic examination showed marked hyperkeratosis and numerous enlarged nerve endings in the corium. No tumor cells and no xanthoma cells were visible with stains for fat.

#### DISCUSSION

DR. S. W. BECKER: I thought I saw some hyaline degeneration in the section of the nerve itself, not a neuroma in the sense of nerve proliferation, but indication that the nerves were definitely degenerated, and that might account for the peculiar whitish appearance of the lesions on the ball of the finger. There are swelling, hyaline change and a little fibrosis in the nerve endings but no such changes as occur in real neuromas.

DR. O. H. FOERSTER, Milwaukee: I recently saw a patient who had a history indicating that the tips of three fingers on each hand at one time were swollen and indurated and, furthermore, that the tendon sheaths of the fingers were stiffened. Several years later, when my co-workers and I saw her, we found atrophy and calcareous nodules in the tips of the fingers, the flexor tendons were shortened, and the picture was that of a sclerodermatous process. That might be a suggestion for diagnosis in Dr. Zeisler's case. There was no opportunity for biopsy in the case to which I referred.

DR. E. P. ZEISLER: I think that the disorder is some rare condition involving the tendon sheaths and causing hypertrophy of the finger, it is evidently not xanthoma or tuberculosis. The patient is in good health, and the lesion is not painful. I thought it might be a neuroma.

### A CASE FOR DIAGNOSIS Presented by DR. OLIVER S. ORMSBY

This man, aged 65, presents an eruption of three months' duration. He has had psoriasis for twenty years, for which he has received no treatment. When this new eruption appeared there were patches of psoriasis on the extensor surface of the right forearm and over the lower portion of the spine and one small patch on the left side of the abdomen. The new eruption was rather generalized, affecting the extremities and the trunk, and was accompanied by marked pruritus.

At the time of the first examination, on Oct. 23, 1935, numerous nummular and larger bluish-red plaques were noted. The margins of several were raised and infiltrated. Irregularly scattered bullae were present, particularly on the thighs and forearms. During the month in which the patient has been under observation no new lesions other than bullae have developed, but the bullae are much more numerous than they were in the beginning.

Today, over the covered portions of the body there are numerous circular and polycyclic lesions from the size of a pea to that of a palm with raised, bluish-red

borders. Some of the patches have normal skin in the center, others present a yellowish-brown hue. There are numerous bullae of variable size on the margins of the lesions. Over the sacrum and extensor surface of the right forearm there are ordinary patches of psoriasis.

The differential leukocyte count gave the following results: polymorphonuclear leukocytes, 50 per cent, lymphocytes, 31 per cent, eosinophils, 9 per cent, monocytes, 10 per cent.

## DISCUSSION

DR UDO J. WILE, Ann Arbor, Mich. My impression is that there are two separate conditions, although it would be simpler if one could explain the bullae in the old lesions of psoriasis on the basis of the psoriasis. I do not think that that is altogether possible. I wonder whether this patient is taking something, such as iodine, which produces the bullous formation or whether this case is an instance of Duhring's disease developing in a patient with psoriasis. I think that in view of the serpiginous outline of the lesions on the thigh which are not scaling, a diagnosis of some form of bullous erythema in the course of psoriasis offers the most satisfactory solution.

DR EDWARD A. SKOLNIK. I saw this patient two months ago, and the physician who referred him stated that physical examination and studies of the urine and of the blood gave essentially negative results. The chief complaint at that time was of the severe psoriasis. Examination revealed the psoriasis and a generalized papular eruption, with circinate and bluish discolored plaques on the extensor and flexor surfaces of the forearms. There were no bullae at that time, but about a week later those lesions appeared. I have observed the patient on several occasions, and there has been practically no change except that a few new lesions have appeared. When I saw the patient I thought that the disorder was bullous erythema multiforme, and it now looks practically the same as it did then.

DR CLARK W. FINNERUD. I saw this patient some time ago at my clinic, and my impression was much like that of Dr. Skolnik. The patient had psoriasis and, I thought, also erythema multiforme rather than dermatitis herpetiformis. Later, when I saw him again with Dr. Ormsby on one occasion, there were some areas suggestive of mycosis fungoides, and at that time most of the edematous-looking plaques and bullae had disappeared, but there were some discoid and crescentic, scaling, well infiltrated plaques which were different from his psoriatic lesions.

DR OLIVER S. ORMSBY. The amount of infiltration in the plaques has diminished in the last month, and the number of bullae has increased.

DR O. H. FOERSTER, Milwaukee. The clinical picture on the thighs is that of dermatitis herpetiformis. When one takes into account the changes that have been described as taking place in the eruption, the history that the man has taken liquid petrolatum every day and the dusky appearance of the violaceous border of several of the lesions, I think one must consider phenolphthalein as a possible cause for the condition.

DR WILLIAM ALLEN PUSEY. I think Dr. Wile summarized the case very well. I believe one has to forget that the patient has psoriasis. He has a toxic erythema, but this is one of the cases in which one cannot tell whether the disorder is toxic erythema or a toxic erythema and Duhring's disease.

DR OLIVER S. ORMSBY. I think the discussion is very pertinent, and I believe that the condition will be proved to be bullous erythema multiforme or Duhring's dermatitis herpetiformis. I think that one cannot make a definite diagnosis at present.

LYMPHOBLASTOMA (LEUKAEMIA CUTIS). Presented by DR OLIVER S. ORMSBY.

This man, aged 65, presents a cutaneous disorder of nine months' duration, which began with marked pruritus, followed by generalized erythema and pigmentation.

The entire skin is a deep mahogany brown, the pigmentation being deepest on the trunk. Moderate adenopathy is present. There is no evidence of scaling or traumatic dermatitis from scratching. The patient's general health is good.

The leukocytes numbered 18,000 per cubic millimeter, and the results of the differential count were as follows: polymorphonuclears, 25 per cent, lymphocytes, 73 per cent, and transitional cells, 2 per cent.

#### DISCUSSION

DR UDO J. WILF, Ann Arbor, Mich. I was much interested in seeing this patient, whose condition, I think, can hardly be diagnosed unless the blood is examined. There is little that I can add to the discussion on this subject, which seems to be growing more extensive all the time, except to express my opinion that there are two distinctly different types of lymphoblastoma as seen in the skin. The first type is illustrated by Dr Ormsby's case and consists of a primary condition of the blood with secondary cutaneous manifestations. Cases of this type comprise for the most part those in which a dermatologist sees the patient after an internist has seen him or in which the patient consults a dermatologist because of cutaneous manifestations such as leukemic nodules or other lymphoblastomatous cutaneous lesions. Under this heading are the well known dermatoses seen in association with lymphosarcoma and Hodgkin's disease.

On the other hand, there are cases in which, I believe, a lymphoblastomatous change in the skin as well as in the blood and lymph glands is secondary to certain primary cutaneous insults. This group, I believe, is even larger than that of cases of the essential or primary condition in the blood. In this group one finds cases of ordinary cutaneous disease, such as occasional cases of psoriasis and cases of external dermatitis, in which the disorder becomes universal, leading to exfoliative dermatitis, and during the course of this condition the lymph glands and not infrequently the blood become involved, and the lymphoblastomatous changes take place in the skin itself.

I have repeatedly seen the picture develop in this way, and I am convinced that one can definitely separate these two groups of cases. The cases of primary or essential lymphoblastoma are usually fatal. Recovery, however, may occasionally take place in the cases of secondary lymphoblastoma, and remission is much more common in them.

DR OLIVER S. ORMSBY. This is the fourth patient with identical signs whom I have presented. My co-workers and I have been able to make a probable diagnosis before examining the blood. One of the patients suffered intensely, and more than eighteen months elapsed before any changes in the blood occurred. Then extensive adenopathy developed, and the patient died within a year of leukemic changes in the blood and erythroderma. I think it is important that one is able to recognize such an important disease merely by the appearance on the skin of a particular type of erythema.

#### A CASE FOR DIAGNOSIS (KAPOSI'S SARCOMA?) Presented by DR THEODORE CORNBLEET

A L., a man aged 67, first noticed an eruption on his right leg eight years ago. The eruption increased slowly in extent, but in the last two months there has been more rapid extension.

At present the eruption consists of slate-gray to red nodules and large nodes, the largest of which is the size of a small walnut, practically all the lesions remain intact, and some of them are covered with a scaling crust. They are somewhat firm, indurated and sharply elevated and are accompanied by no subjective symptoms. No lesions have appeared on the palms or soles, except for one that formed two weeks ago on the plantar surface of the right great toe and was quite painful for several days. The patient's health has been good, and a general examination revealed no abnormalities.



Examination of the blood showed a number of young forms among the white cells, but their total number and differentiation were within normal limits

This man has been treated by experienced dermatologists and has attended a number of well known clinics in the country. Reports from several of them showed a leaning toward a diagnosis of Kaposi's sarcoma. He is presented because a section made by some one else was examined at Dr Cornbleet's request by Dr Richard Jaffe, pathologist of the Cook County Hospital. Dr Jaffe said that as far as he could see on the one section and with the reservations enforced by the lack of opportunity for making special stains (no tissue being available) the disorder was a leiomyoma. He thought that the part which had been regarded as whorls of connective tissue was in reality smooth muscle, and he advised that this diagnosis be corroborated by special stains. The one slide available showed neither areas of hemorrhage nor pigmentation. There was, however, new formation of blood vessels.

#### DISCUSSION

DR CLARK W. FINNFRUD. I think that the disorder is Kaposi's sarcoma. The clinical appearance of the lesions is characteristic, even down to the warty appearance at the sides of the dorsa of the toes. As to the nuclei in the cells which resemble myoma, I have seen nuclei of that size, shape and situation in purely fibrous hypertrophy.

DR RUBEN NOMLAND. In spite of the apparent lack of pigmentation in the microscopic section, the architecture—the intertwining of cells of the elongated type—is typical of Kaposi's sarcoma. I think that perhaps special staining of other portions of the lesion for iron would demonstrate the presence of hemosiderin.

DR DAVID LIEBERTHAL. The disorder is clinically typical of Kaposi's sarcoma, especially the lesions on the distal parts of the lower extremities. As regards the microscopic diagnosis, I should say that it is too much to ask of any one to make it after a hurried glance at the sections. But I am certain that if the sections were studied carefully the histologic picture would support the clinical diagnosis of Kaposi's sarcoma.

DR JAMES H. MITCHELL. In the patient I have presented here on two occasions with lesions on the hands a number of additional lesions have developed on the feet and recently one lesion has appeared in the mouth. The lesion in the mouth is clinically the same as the other lesions, being vascular and tender. I should like to know whether any of the members has seen an early lesion of Kaposi's sarcoma in the mucous membrane of the mouth.

DR THEODORE CORNBLEET. I am grateful for the discussion. I have not had an opportunity to take a specimen for biopsy as yet, but I hope to obtain material from one of the nodules and use some special stains, this should be done in order to rule out the possibility of the lesions, being fibrous tumors or muscle tumors. I shall use Van Gieson's stain and blue stains as well.

DR WILLIAM ALLEN PUSFY. I am willing to make a positive diagnosis of Kaposi's sarcoma without waiting for further examination.

A CASE FOR DIAGNOSIS. Presented by DR F. E. SENEAR, DR W. K. FORD, and DR MARCUS R. CARO.

L. S., a woman aged 36, presents several pea-sized dull red solid nodules on the right ear, they are located chiefly on the concha and anthelix, and one extends into the oral canal. The lesions have been present for about two years, they are symptomless but occasionally become crusted after scratching. Several nodules have been removed by actual cautery.

The Kahn reaction was negative. Examination of the blood showed 75 per cent hemoglobin, and 10,200 leukocytes with 67 per cent polymorphonuclear neutrophils, 25 per cent lymphocytes, 6 per cent monocytes and 2 per cent eosinophils. Urinalysis gave negative results.

Histologic examination revealed acanthosis of the epidermis except for a small central ulcer. In the center of the lesion the corium contained many dilated blood vessels, each surrounded by a thick, edematous fibrous mantle. At the sides the vessels were less markedly dilated and were surrounded by densely packed mantles of histiocytes, lymphocytes and plasma cells. Stains for tubercle bacilli and fat gave negative results.

## DISCUSSION

DR RUBEN NOMLAND. I have had the opportunity of doing two biopsies on lesions that were clinically what is called solid edema, that is, recurrent attacks of streptococcal infection, and one of those disorders involved the ear. The section from that lesion was a duplicate of the section shown. There was dilatation of the lymph spaces and a reaction of tubercloid type. I think this could be the result of a simple inflammatory reaction rather than of some specific granuloma.

DR WILLIAM ALLEN PUSRY. That seems to me to be a logical conception of the situation, but how does Dr. Nomland account for the persistence of this inflammatory process and the edema?

DR RUBEN NOMLAND. In cases of similar disorders there has been a history of recurrent attacks of cellulitis, and the lesions presented the same clinical and microscopic picture. I think the disorder need not be classified as specific.

DR MARCUS R. CARO. I agree with Dr. Nomland's interpretation of the histologic observations. All I could make out was simple inflammatory reaction. The clinical history does not include any attacks of acute inflammation, which ordinarily would be present with recurrent cellulitis, therefore we still leave the diagnosis open.

#### A CASE FOR DIAGNOSIS (SENSITIZATION PLUS INFECTIOUS DERMATITIS?) Presented by DR. CLARK W. FINNERUD

This man, aged 31, a milling machine operator, presents a mildly pruritic eruption of the dorsa of the hands, left cubital fossa, flexor surfaces of the forearms, elbows, upper lip, sides and front of the neck and right leg, of three weeks' duration. There is no history of previous cutaneous disorder. The general history, except for a gastric ulcer in recent years, is irrelevant. The patient states that for the past eighteen months he has been working at a machine which splashed considerable oil of cloudy, almost milky, appearance.

The patient presents a scaling, bluish-red eruption almost diffusely involving the dorsal surface of the hands and a somewhat lichenoid discrete papular involvement of the flexor surface of the forearms. A similar, but more diffuse and partially linear, papular eruption is present in the left cubital fossa and on the front and sides of the neck. There is a mild erythematous, scaling dermatitis on the face, and the upper lip is the site of a sharply demarcated area of crusting dermatitis, sycosiform in appearance. A psoriasiform plaque is present on each elbow, and an area of crusting dermatitis the size of a hand or larger, on the front of the right leg. There is a patchy erythematous scaling dermatitis at the base of the penis and in the pubic region.

The Wassermann reaction of the blood was negative. The patient has not obtained a sample of the oil for patch testing.

## DISCUSSION

DR CLARK W. FINNERUD. Only today I noticed that there is intertriginous involvement of the first interspace of the right foot, but I think that this suggestive mycotic element does not account for the entire picture.

DR HOWARD J. PARKHURST, Toledo, Ohio. I wonder whether examinations for fungi have been made. It impressed me as perhaps more likely, if any of the disorder is due to fungi, that part of it might be a secondary toxic manifestation.

DR LESTER M. WIEDER, Milwaukee. This patient also has lesions of the eyelids, which, he told me, have been present for six months, apparently preceding

the other lesions. Much of the disorder is intertriginous, except for the dorsal surface of the hands, elbows and shins. He stated that the lesion of the right shin began as a patch which extended peripherally. I believe that the disorder is either of mycotic or of bacterial—probably of mycotic—etiology and that some of the smaller papular lesions may be "ids" or toxic lesions. On the shoulders and in the axillary folds there are numerous scaling follicular papules, which, I thought, might be toxic lesions of this type. I think that a microscopic examination should be made of the material from lesions on the foot, and an intracutaneous injection for diagnostic purpose might be tried also.

DR CLARK W. FINNERUD. I appreciate the suggestion that this might well be an infection with *Monilia*, but it is a little hard for me to conceive how that might account for the lesions on the elbow and for those on the face and neck. The eruption in the genital area is practically limited to the pubic region and the groin. I shall certainly try to demonstrate fungi, at least between the toes and in the crotch.

NOTE.—Cultures and fresh preparations in potassium hydroxide from all the involved areas gave negative results for yeast and yeastlike fungi.

#### A CASE FOR DIAGNOSIS. Presented by DR MARCUS R. CARO

P. P., a woman aged 33, is presented by courtesy of the Mandel Clinic. She states that lesions appeared on her neck about six years ago. Since then the eruption has gradually extended, involving the entire neck, the upper part of the chest and, to a lesser extent, the loins. Pruritus is severe in warm weather, especially at night.

The eruption consists of many closely aggregated papules the size of a pin-head and slightly larger. The lesions are chiefly flat, but a few are globular, they are round or angular and shiny and vary in color from flesh color to slightly more reddish. There is no enlargement of the lymph glands. The patient states that her sister has had a similar eruption for several years.

Examination of the blood gave the following results: The Wassermann reaction was negative, the hemoglobin content was 80 per cent, the leukocytes numbered 13,000 per cubic millimeter, and the differential count showed 53 per cent polymorphonuclear neutrophils, 44 per cent lymphocytes, 1 per cent monocytes and 2 per cent basophils. Urinalysis gave negative results.

Histologic examination of a biopsy specimen taken from the neck showed a dermal papule over which the epidermis was slightly flattened. In the center of the papule just beneath the epidermis the connective tissue was diffusely infiltrated by histiocytes, lymphocytes and free red corpuscles. Below this zone and extending deeply into the corium lay many sharply circumscribed, densely packed cellular nests. In each of these the walls of the blood vessels showed proliferation, amounting even to complete obliteration of the lumen. Within the walls and about the vessels lay concentric layers of histiocytes and lymphocytes, with occasional free red corpuscles, all densely packed together but separated by remaining fine strands of collagen fibers. Many large brown chromatophores were present within these nests and in the intervening corium. Staining of sections for tubercle bacilli, amyloid and fat gave negative results.

#### CLUTTON'S JOINT, ASYMMETRICAL (HYDRARTHROSIS). Presented by DR M. DORNI and DR S. J. ZAKON (by invitation)

Miss D., aged 24, American of Polish descent, went to the clinic of the Mount Sinai Hospital on Sept. 9, 1935, because of pain in the right eye. Examination by the ophthalmologist disclosed acute interstitial keratitis. The Wassermann reaction of the blood was positive, and the patient was referred to the clinic for syphilitic patients. Examination in that department on September 25 revealed interstitial keratitis affecting the right eye. Hutchinson's teeth and swelling of the left knee, which was twice the size of the right, the swelling extending into the

soft tissues of the thigh and leg. The patient stated that the swelling had been present for seven months before the appearance of the interstitial keratitis but that it was painless and did not interfere with movement. Roentgenograms showed no involvement of the bones. The serologic reaction of the blood of the patient's mother was strongly positive.

The patient was given bismuth subsalicylate, and after three injections there was complete disappearance of the swelling in the knee joint.

## DISCUSSION

DR S. J. ZAKON (by invitation). The object in presenting the patient was to show that swelling of the knee joint in patients with Clutton's hydrarthrosis is not necessarily symmetrical. Klauder (Klauder, Joseph V. and Robertson, Harold F. *J. A. M. A.* **103**:236 [July 28] 1934) stated that this condition does not respond readily to treatment, but in this patient it responded well to two or three mild treatments.

ERYTHEMA ANNULARE CENTRIFUGUM. Presented by DR E. P. ZIEGLER and DR MARCUS R. CARO.

L. L., a girl aged 5 years, had a small ringlike lesion on the back of the left thigh about eight months ago. The lesion was treated with carbon dioxide snow and nearly disappeared. Recently it has been growing larger, and it shows activity in the slightly elevated, dull reddish border.

## DISCUSSION

DR FREDERICK R. SCHMIDT. Recently Dr Ormsby discussed four types of atypical erythemas. The fourth type, I think, is called erythema gyratum simplex. My impression is that this lesion is not one of erythema annulare centrifugum but that it fits in better with a disorder I saw described as erythema gyratum simplex. I cannot remember the name of the author who described it.

DR MARCUS R. CARO. I believe this is just a form of localized toxic erythema in annular formation.

A CASE FOR DIAGNOSIS (PERSISTENT SYMMETRICAL ERYTHMATOUS EDEMA OF THE FACE). Presented by DR JAMES H. MITCHELL.

This woman, aged 38, was first seen on Aug. 28, 1935, at which time the condition had existed for six months. She states that it began as a small area of erythema, which has gradually enlarged, and that the eruption was accompanied by little, if any, sensation. There was marked variation in the erythema and some in the edema. Definition had remained constant. The patient was seen a few times at the Central Free Dispensary but has refused to return because a vesicular eruption appeared on her legs after she received an injection of sodium thiosulfate. She admits that before this vesicular eruption appeared she had been walking in the woods.

The patient was referred by Dr. Nelson Percy, who reported that a complete physical examination had revealed nothing abnormal. Since the patient came under observation she has been given local treatment with a soothing ointment, one treatment with roentgen rays and one injection of 0.025 Gm. of gold and sodium thiosulfate, followed by a second injection of 0.05 Gm. with no benefit.

Examination of the blood showed 4,760,000 erythrocytes and 9,400 leukocytes. The blood pressure was 130 systolic and 34 diastolic. Examination of the urine showed an acid reaction and no albumin and sugar; microscopic examination showed from 4 to 8 pus cells per field, a few blood cells and no casts.

## DISCUSSION

DR CLARK W. FINNERUD. I treated a patient with a like condition at the time gold and sodium thiosulfate was first used. I thought the disorder was lupus

erythematosis, and in the beginning I used a few injections of sodium thiosulfate and then changed to gold and sodium thiosulfate therapy. A severe reaction developed, the patient was in bed with a high fever for several weeks, and the eruption became generalized. Subsequently it cleared entirely with local application of mild preparations and intravenous administration of sodium thiosulfate.

DR E P ZEISLER The patient presents the clinical appearance of what Kaposi called *crispelas perstans faciei*. In the majority of cases the condition turned out to be acute lupus erythematosis.

DR DAVID LIEBERTHAL I am strongly inclined to support the diagnosis of lupus erythematosis. And in connection with the mention of treatment with a gold preparation I wish to call attention to the sodium gold double salt of an amino-arylphosphinic acid. I have been using this preparation in preference to other gold compounds. It has given me good results, and I have not seen any serious reactions from it.

DR WILLIAM ALLEN PUSEY The disorder seems to me a beginning of solid edema of the face. There are persistent lymphangitis and edema that persists at times. I believe the condition will gradually become worse.

DR JAMES H MITCHELL There are several reasons why I have withheld treatment. In the first place, the patient showed unmistakable signs of making trouble for the dispensary. I kept her pacified as well as I could. Another reason has been that she has a tendency to make trouble for me, and I wished to observe her and see how the disorder would progress. I thought there was a possibility of its becoming lupus erythematosis. I remember a patient in Dr Ormsby's practice with a somewhat similar disorder which later changed to lupus erythematosis. The obvious thing is that there is some focal infection about the face. The physician who referred the patient to me examined her thoroughly and found nothing abnormal about the head or neck. Another possibility is the Libman-Sachs syndrome, but there is no sign of that. I gave two very small doses of gold and sodium thiosulfate, and the patient complained bitterly of the reaction. I did not see it, but she told me about it by telephone.

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MAX S WIEN, M D, *Secretary*

*Regular Meeting, Dec 18, 1935*

WILLIAM ALLEN PUSEY, M D, *President, Presiding*

#### A CASE FOR DIAGNOSIS Presented by DR E A OLIVER

This man, aged 35, was first seen by me on Oct 18, 1935, because of a large indurated lesion on the lower portion of the back just to the left of the vertebral column. The patient states that his wife first noticed this lesion about two and a half years ago. There was no pain or pruritus and the patient was conscious of the swelling only when the back of his office chair rubbed against it. By wearing a large pad over the lesion he was able to protect it.

There is an indurated swelling 3 inches (7.5 cm) long by 1½ inches (3.8 cm) wide just to the left of the vertebral column in the lower portion of the back. The lesion is red and nodular.

#### DISCUSSION

DR UDO J WILE, Ann Arbor, Mich I think this lesion has many of the characteristics of a metastasis from a malignant neoplasm. It reminds me of the large plaques in the skin that occasionally follow scirrhous carcinoma of the breast. This possibility, of course, could be easily substantiated by a biopsy, and I assume that one will be made.

DR RUBEN NOMLAND A specimen for biopsy was obtained, but unfortunately the tissue was not excised quite deep enough. Most of that which was obtained was made up of the connective tissue capsule about the tumor. However in several places there were cells which looked like tumor cells that had contained a great deal of lipoid material. I believe that the lesion is a tumor of the chromaffin tissue, probably a hypernephroma.

DR HAMILTON MONTGOMERY, Rochester, Minn. I did not see enough in the section presented to enable one to make a diagnosis. There were some tumor cells present but not enough other features to suggest a hypernephroma. The section does not extend deeply enough. I believe that it would be much better to take another specimen for biopsy than to hazard a pathologic diagnosis on the basis of these inconclusive observations.

DR WILLIAM ALLAN PUSIS I thought as does Dr. Wile, that the tumor was probably a metastatic process, but I did not see the resemblance to carcinoma that he saw.

DR E. A. OLIVER I believe, as Dr. Wile does, that the lesion is a metastatic tumor of some type. It has been growing very slowly for two and a half years, hence it cannot be highly malignant. When Dr. Nomland suggested that a portion of it resembled hypernephroma tissue, I talked to several urologists and they told me that such tumors are not uncommon. The patient has promised to return to allow me to get a deeper specimen for biopsy. All that has been done so far is a complete urinalysis and a Wassermann test, both of which gave negative results. I shall try to present the patient in January with a complete diagnosis.

#### FIXED ERUPTION OF ERYTHEMA MULTIFORME TYPE, APPARENTLY NOT DUE TO INGESTION OF A DRUG Presented by DR S. W. BICKER

This woman, aged 24, married, was first seen in April 1934. At that time she stated that an eruption had appeared six times since September of the preceding year, each attack usually lasting about two weeks. In the beginning the lesions were limited to the lips and genitalia, but in subsequent attacks they involved the hands. The eruption consisted of bullous lesions located about the lips, mouth and genitalia, with erythematous plaques on the hands and arms. The patient stated that the identical regions were involved in each attack and that one lesion on the left side of the forehead was always present. Subsequent attacks became increasingly severe, and the condition was gradually extending.

Blood serum was sent to Dr. Welsh at the Mayo Clinic, it showed a negative reaction with antigen of erythema multiforme and a positive reaction with antigen of pemphigus.

The present attack began two weeks ago, and the lesions are now involuting.

Careful questioning of the patient regarding ingestion of drugs revealed nothing significant. No foci of infection could be found. Examination in the gynecological clinic showed slight mucoid discharge but no pelvic abnormality. The Kolmer and Kahn tests of the blood serum and examination of the urine gave negative results. The blood pressure was 120 systolic and 64 diastolic.

#### DISCUSSION

DR E. A. OLIVER I saw this patient about a year ago in my office, and at that time I thought that the disorder was a severe multiform erythema. The lesions were present principally on the mucous membrane. The mouth and throat were full of lesions, and there were a number about the vulva and vagina. When I first saw the patient she was much excited because she had just come from the office of a physician who had made a diagnosis of secondary syphilis. I advised her to have all foci of infection removed, and today I learned that she had her tonsils removed, without benefit.

DR UDO J. WILE, Ann Arbor, Mich. In reference to the difficulty in eliminating drugs as sources of fixed eruptions, I do not know how new this is to the members, but there are one or two substances closely related to phenolphthalein

that are not taken as drugs but that, as I have observed in the last six months, have produced changes analogous to those caused by phenolphthalein, particularly in the genitalia and mouth. One of these is erythrosin, which is largely used in coloring dentifrices and is also used as a coloring and flavoring, in the form of grenadine. All these syrups, so far as I know, are not made with erythrosin, but in one of the cases I investigated no pink substance other than the grenadine syrup had been ingested, and it was colored with this material. I am also told that bakers are using this erythrosin as a coloring material for icings, and it is not at all impossible that many of the fixed eruptions may also be due to this preparation.

DR S W BECKER. I questioned the patient carefully, and she stated that she is certain that in each attack each lesion that was present in the previous attack has reappeared in the next attack but that each attack has been more severe than the preceding one and that the lesions have increased in number. She has one lesion on the forehead which, she states, has been present in each attack.

DR OLIVER S ORMSBY. It might be of some interest in this connection to refer to a patient with multiform erythema whom I saw yesterday. That patient had recurrent attacks in which the lesions were for the most part limited to the mouth. There had been some lesions on the extremities, but they were not like an eruption due to phenolphthalein. The patient was seen some time ago by Dr Wile, when the lesions presented the appearance of an eruption due to phenolphthalein so he tested the patient with that drug, and this was followed by an exacerbation. Since that time the progress of the eruption has been such that it seems that phenolphthalein could be ruled out, unless it has been taken in some of the other forms mentioned today. One must recognize that erythema multiforme presents a multiform group of symptoms which sometimes simulate one disease and sometimes another. I do not know any instance in which this was demonstrated more plainly than in the case of the patient I presented last month and showed photographs of today. It is known that patients with erythema multiforme present several types of lesions and that sometimes a distinction between erythema multiforme, dermatitis herpetiformis and pemphigus is difficult if not impossible.

DR S W BECKER. I appreciate the information Dr Wile has given, for this is the third patient who has stated that in each attack the same spots have been involved with the same type of lesion. The first patient was observed through two acute attacks. During the first she was questioned carefully and mentioned the possibility of medicaments' being the cause of the eruption. When she returned at the time of the next attack the most careful questioning elicited no history of ingestion of drugs. The second patient had been seen by two other dermatologists, both of whom had questioned her regarding the ingestion of drugs. That patient was very intelligent, and my co-workers and I tried to elicit a history of ingestion of drugs, but we were entirely unable to obtain one. When the patient who is presented was first seen, in 1934, we made a diagnosis of erythema multiforme, but when she returned about a week ago and stated that more lesions had appeared in some places we went carefully into the history but could get no record of ingestion of drugs. There is an article on fixed erythema that is of interest (Wohlstein, E, and Schmidt, L. Ueber ein fixes Erythem *Dermatol Wchnsch* 89 1766, 1929). The authors stated that up to the time the article was written no one had reported a fixed erythema which was not due to drugs, but they reported the case of a man, aged 48, who had this type of eruption. After all, one realizes that the mechanism of the eruptions due to drugs is not known. The skin itself is not necessarily sensitive to the drug, as has been shown by various scratch and intradermal tests, hence there is no reason why a patient should not exhibit a fixed eruption due to a toxic manifestation from another source. I shall question this patient further regarding the possible use of these dye stuffs and see whether any enlightenment can be obtained.

DR M H EBFRT. I think it would be interesting to get a photograph of the patient during an acute attack in order to have a basis for comparison with future attacks.

DR JAMES H MITCHELL MacKee and Wise described multiforme erythema of the fixed type (*J Cutan Dis* 36 190, 1918) Dr Ormsby may remember a patient seen in the dispensary several years ago who was tested for every substance one could think of but reacted to none Photographs were taken of that patient He had a perfectly classic fixed eruption with thousands of lesions The photograph was in the record and could be referred to at each attack The spots never varied in size, number or location

DR H RATTNER I saw a patient of Dr Pusey who had recurrent attacks of erythema multiforme, one attack was traced to pink toothpaste and one to pink icing on cake

DR OTTO H FOERSTER, Milwaukee Sometimes on close questioning of an intelligent patient as to the use of laxatives, one finds as in the case of one patient who had an eruption undoubtedly due to phenolphthalein, that the patient admits using cascara but insists that he never used phenolphthalein in any form Investigation of the cascara sagrada preparation may show that it is fortified with phenolphthalein

DR HAMILTON MONTGOMERY, Rochester, Minn In my experience it is not unusual for a druggist to put up fluid extract of cascara containing phenolphthalein without mentioning the latter on the label on the bottle

DR WILLIAM ALLEN PUSEY I think it would be impossible for any one to say that he had not taken phenolphthalein in some way It is impossible to eliminate these things with mathematical certainty

DR HARRY M HEDGE When Dr Ganz was here and attended a meeting of the Chicago Dermatological Society at the medical school of Northwestern University I presented a patient who, as was discovered, had an eruption due to bromide For three months at the clinic I had questioned her about the use of drugs or any medication she had been taking, and I had received negative answers each time The only other possibility was that of a blastomycosis I finally presented her with that diagnosis, but when at the meeting she was asked point blank "How do you sleep?" she answered "Very poorly, I have to take a powder every night"

#### EPIDERMOLYSIS BULLOSA WITH HYPERTRICHOSIS AND MELANOSIS Presented by DR M E OBERMAYER

A woman, aged 30, of Canadian and English-American descent, states that about ten years ago, during the summer, blisters developed on the area where the strap of a golf-bag touches the shoulders From that time on similar lesions appeared every summer when she carried a golf-bag on hot days Five years ago bullae developed on the hands, elbows and ankles after slight trauma, and this condition has recurred every year since except during the months from November to April inclusive, during which time the patient has always been free from lesions The bullae vary in size and depth Some have ruptured spontaneously, while the smaller and deep-seated ones have been opened by the patient "in order to relieve the pain" All the lesions left pigmentation, and those on the elbows and ankles left atrophic areas Eight years ago the patient noticed that her skin began to darken and that the hair on the face, legs and arms began to grow Her libido is normal She states that she had menstrual irregularities up to the time of her marriage So far as she knows, no member of her family has ever had a similar condition There is no blood relationship between her parents

Roentgen examination revealed no abnormality in the pelvis or sella turcica A bilateral pyelogram showed normal conditions The dextrose tolerance test gave negative results The basal metabolic rate was -10 per cent The blood pressure was 114 systolic and 73 diastolic A differential count showed that the number of lymphocytes was slightly increased, the count revealing 43 per cent

The experimental production of bullae by the application of ultraviolet radiation and friction was tried repeatedly without success on various parts of the body



The intradermal injection of serum from the blisters with saline solution as a control also gave negative results

The patient has been using hot wax for depilation of the face and has had no cutaneous reaction

## DISCUSSION

DR WILLIAM ALLEN PUSEY The patient seems to present an interesting set of symptoms (1) epidermolysis bullosa, (2) the abnormal pigmentation and (3) hypertrichosis I regard all these conditions as anomalies of development

DR M E OBERMAYER This case is interesting for the reason Dr Pusey has pointed out The almost simultaneous onset of the eruption and of melanosis and hypertrichosis is in line with Guy's suggestion that epidermolysis bullosa represents a congenital polyglandular syndrome Interesting also is the late onset which suggests the acquired or tardy form of the disease as described by McLeod The absence of heredity indicates that the mode of transmission in this case is not dominant but recessive, a feature which is unusual in the dystrophic type of the disease Studies of the hematoporphyrin content of the urine will be made later

## A CASE FOR DIAGNOSIS Presented by DR OLIVER S ORMSBY

This patient was presented at the meeting of the Chicago Dermatological Society in November, and the history is given in the proceedings of that meeting (ARCH DERMAT & SYPH 33 1081 [June] 1936)

Dr Ormsby presented photographs of this patient to show the progress of the disorder since the first presentation

Within two or three days after presentation the lesions on the abdomen began to enlarge, and the circles covered the entire trunk Then near the center of the old lesions other rings started and enlarged peripherally, just as they do in erythema perstans The bullous lesions gradually disappeared, and intravenous injections of calcium cleared up the disorder About one week ago, when the disorder had almost entirely cleared up, it was noted that the number of eosinophils had increased to 36 per cent

## CLEVELAND DERMATOLOGICAL SOCIETY

J R DRIVER, M D, *Reporter*

*Regular Meeting, June 27, 1935*

R E BARNES, M D, *Presiding*

## DESTRUCTIVE GRANULOMA OF THE NOSE. Presented by DR W H CONNOR

C H, a man aged 42, from the service of Dr Cole and Dr Driver at the City Hospital, was presented before this society in March 1932 (ARCH DERMAT & SYPH 26 773 [Oct] 1932), at which time he was admitted to the hospital because of an extragenital chancre of the chin, associated with a generalized secondary eruption on the body At that time the patient was receiving treatment for secondary syphilis It was noted that there was an ulcerative process involving the right ala nasi, this, according to the patient, had been progressing slowly for five or six years Antisyphilitic treatment had no effect on the lesion of the nose The possibility of rhinoscleroma was considered, but as the patient did not come from Austria or southern Russia there was slight probability of that disorder, and subsequently examination of smears for the bacillus of rhinoscleroma gave negative results The involvement has become progressively worse, and the patient now presents a marked destruction of the septal and of the alar cartilage associated with ulceration The Wassermann test of the blood is now negative,

and roentgenograms show no evidence of tuberculosis of the lungs and no destruction of the bones in the nose. Examination of smears for tubercle bacilli gave negative results. A tuberculin test was positive with a dilution of 1:10,000.

Biopsy showed a hyperplastic epithelium with enlarged, prolonged rete pegs. Nuclear elements were vesicular, and spongiosis was present. In the corium there was a localized extensive inflammatory infiltrate of round cells with considerable edema. There were many new blood vessels and fibroblasts. A pathologic diagnosis of chronic granulomatous inflammation was made.

Except for application of local antiseptics, no treatment has been given, and no improvement has been noted.

#### DISCUSSION

DR JOHN E. RAUSCHKOLB: My co-workers and I have observed this patient off and on since 1932. The condition of the nose has progressed slowly. The clinical picture suggests that the lesion may be a gumma. However, as we saw the patient when he had an early stage of syphilis and as the process on his nose had been present for several years before that, we know that the lesion is not due to syphilis. Ulceration due to phosphorus might have to be considered, but the patient has never worked with phosphorus. Studies for rhinoscleroma have given negative results. We are still unable to make a diagnosis.

DR R. E. BARNEY: If the disease were rhinoscleroma, there would hardly be so much destruction of the tissue. The lesion of rhinoscleroma is usually a hard, infiltrated, shiny plaque.

DR J. R. DRIVER: On account of the slow progress of this disease and in view of the fact that the patient has a positive reaction to tuberculin, I am inclined to believe that the disorder is tuberculosis, a destructive form of lupus vulgaris. The histologic picture does not exclude this diagnosis. Certainly there is a granulomatous process, and evidence has shown that it is not malignant and that it is not due to syphilis.

#### HEREDOSYPHILIS Presented by DR W. H. CONNOR

A girl, aged 4 years, from the service of Dr. Cole and Dr. Driver at the City Hospital, nine months ago began to suffer from convulsions and progressive loss of speech associated with choreiform movements. Neurologic examination revealed spasticity of the muscles and incoordination. There were no ocular symptoms, and encephalography showed no abnormalities. Examination of the spinal fluid gave negative results in all respects. The cell count was within normal limits. The Wassermann test of the blood was strongly positive. Therapy consisting of weekly injections of acetarsone for nine months was of no benefit.

A boy, aged 14, from the service of Dr. Cole and Dr. Driver at the City Hospital, presents symptoms of juvenile dementia paralytica; he has slurring speech, tremor of the hands and tongue, sluggish pupils and hyperactive reflexes. The Wassermann test of the spinal fluid gave strongly positive results in amounts as low as 0.1 cc. A test for globulin gave moderately positive results, the colloidal gold curve was of the first zone type. The Wassermann test of the blood was strongly positive. Since October 1934 the patient has received eighteen injections of typhoid vaccine for the production of fever and 946 Gm of acetarsone. In addition to this he has received ten treatments with the Kettering hypotherm. No definite improvement has resulted.

A Negro boy, aged 15, from the Service of Dr. Cole and Dr. Driver at the City Hospital, presents interstitial keratitis and iritis and hydrarthrosis (Clutton's joints). The enlargement of the knee joints has been present for about one year. There is a history of repeated attacks of interstitial keratitis and iritis. The Wassermann test of the blood was strongly positive. Examination of the spinal fluid gave negative results. Five treatments in the Kettering hypotherm, totaling twenty-five hours, with a temperature ranging from 105 to 107 F, produced great improvement of the ocular condition. The hydrarthrosis of the knee joints has improved slightly.

A Negro boy, aged 15 from the service of Dr Cole and Dr Driver at the City Hospital, suffers from heredosyphilis, interstitial keratitis, iritis of the right eye and hydrarthrosis (Clutton's joints). Both knee joints are swollen and tender, and fluid is present in each. Both wrists are involved similarly but to a less degree. Weekly intramuscular injections of neoarsphenamine and a preparation of bismuth and internal administration of potassium iodide continued for several weeks have produced little or no improvement. After six treatments in the Kettering hypotherm the interstitial keratitis and iritis have practically disappeared, and there has been slight improvement in the symptoms in the joints. The Wassermann test of the blood was strongly positive, the spinal fluid was normal.

SYRINGOMYELIA ASSOCIATED WITH TROPHIC DESTRUCTIVE BULLAE Presented by  
DR R. E. BARNEY

M. W., a woman aged 41, has a lesion about  $\frac{1}{2}$  inch (1.27 cm.) below the base of the index finger on the dorsum of the left hand, which began five years ago as a "blister." In the past three years about nine similar lesions have appeared over the left shoulder and left anterior portion of the chest. On involution all the lesions leave scars. The patient has had difficulty in using her shoulder joints for the past two years, she complains that her throat has been dry for about three years and that for the past year there has been dysphagia off and on.

The patient is rather obese and short. On the flexor aspect of the junction of the middle and the lower third of the left forearm is an area of superficial ulceration, measuring 4 by 6 cm., it is surrounded by a dusky, erythematous border  $\frac{1}{4}$  inch (0.64 cm.) wide. Here the frayed epidermis gives evidence of a pre-existing bullous lesion. The ulcer proper is covered by a grayish-white exudate. On the dorsum of the left hand, left shoulder and left breast are nine scars of previous lesions from the size of a pea to that of a dollar. The largest scar involves the left breast. There is a linear scar, 4 inches (10 cm.) long, on the extensor aspect of the upper third of the left arm, resulting from an exploratory operation. There is diminution of all types of sensation, but chiefly loss of pain and temperature in the areas supplied by the lower cervical and first seven thoracic nerves on the left side only. There is no definite motor change, save a slight muscular atrophy due to disuse. The grip of the left hand is strong. The tendon reflexes of the left arm are absent. There is no muscular fibrillation. The left arm is slightly shorter than the right. In a sitting position the patient can raise the left arm only about 45 degrees.

The Wassermann test of the blood and examination of the spinal fluid gave negative results. Roentgen examination in November 1934 revealed no widening of the mediastinal shadow. The proximal end of the shaft of the humerus was about 4 inches (10 cm.) from the glenoid cavity. On the slightest muscular exertion the end of the humerus was seen to be brought up into the glenoid cavity. There was absence of the head, tuberosities and upper portion of the shaft of the left humerus. There was some calcification in the soft tissue surrounding the glenoid cavity. The margins of the glenoid and probably the neck of the scapula were also absorbed. A roentgenogram of the esophagus revealed no changes.

Slight improvement has followed roentgen therapy.

#### DISCUSSION

DR H. G. MISKJIAN: I wish to ask the presenter on what basis the diagnosis of syringomyelia was made?

DR E. W. NETHERTON: The roentgenogram showed the destructive process to be in the upper end of the humerus and revealed a sharp line, suggesting that a portion of the bone had been removed at operation. I wish to know whether this is true or whether the defect is a result of the disease. I believe that in cases of syringomyelia of as long standing as this patient's is one would expect to see more deformity, whitlows and similar lesions. I suggest the possibility of a dermatitis artefacta.

DR R E BARNY I realize that a number of symptoms are apparently lacking in order to establish a diagnosis of syringomyelia, moreover, the unilateral distribution does not agree with that diagnosis. One would expect bilateral involvement by this time. Again, there is an absence of whitlows and of deformity of the hand. There are no erythematous areas, cyanosis, etc. The possibility of a tumor involving the posterior nerves or the posterior horn has been considered. The bullous lesions which have developed from time to time have had somewhat of the appearance of a dermatitis artefacta. However, taking all the factors into consideration, I believe that a diagnosis of syringomyelia better explains the condition.

## BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M D, *Secretary*

*Regular Meeting, Nov. 27, 1935*

EUGENE F. KELLER, M D, *President*

FOLLICULITIS DECALVANS ET ATROPHICANS (LITTLE) Presented by DR SAMUEL FELDMAN

W. B., a woman aged 46, has an irrelevant history except for an attack of acute colitis in May 1935. About the end of July of the same year, she noticed that the hair of the scalp was falling out. The loss of hair became gradually worse, and when the patient was examined on Oct. 15, 1935, she presented many small areas of baldness scattered over the scalp. These bald spots were smooth, round and slightly depressed. The follicles between the affected areas were hyperkeratotic, and the hairs, when present, were surrounded by a horny collar at their base.

The patient received two roentgen exposures of  $\frac{1}{2}$  skin unit (50 roentgens) at an interval of one week, this treatment was followed by weekly ultraviolet irradiation from a quartz mercury vapor glow lamp. The keratosis became markedly diminished, but the hair continued to fall out. At present the areas of alopecia are larger, some spots are smooth and slightly atrophic while others present dilated follicles. In the occipital region there are areas of baldness showing definite perifollicular inflammation as evidenced by redness of the follicular rim.

### DISCUSSION

DR DAVID BLOOM Because of the irregular shiny areas of alopecia with scarring, I suggest the diagnosis of healed favus.

DR ADOLPH ROSTENBERG The disorder is evidently a folliculitis ending in atrophy and a loss of hair. It is therefore my impression that it is folliculitis decalvans.

DR VAN ALSTYNE H. CORNELL I also think that the disorder is folliculitis decalvans, although the possibility of lupus erythematosus must be considered.

DR F. E. CROSS I think that the suggestions of Dr. Cornell are tenable. I do not agree with Dr. Bloom's diagnosis of favus in view of the fact that favus is more widespread over the scalp and that the areas of atrophy are not as irregular as in this case. Perhaps Dr. Feldman can give some information on the question of a history of favus. To me the disorder suggests pseudopelade.

DR SAMUEL FELDMAN I expected a difference of opinion because so few cases of this disorder have been reported and the differential diagnosis has not been sufficiently stressed. The condition that this patient presents belongs to a group which has not as yet been properly classified. The condition was described by Graham Little as folliculitis decalvans et atrophicans. I discussed this condition

under the title of lichen planus et accuminatus atrophicans (*ARCH DERMAT & SYPH* 5 102 [Jan] 1922) since in most of the cases definite lesions of lichen planus were seen, and my conception is that the process is a variation of lichen planus. Little in a personal communication stated that he agrees with my view. This patient certainly has no folliculitis decalvans. There are no pustules and there have not been any at any time and there is no scarring. On the other hand, there are atrophy and horny plugs, the conditions described by Little and by me. The differences consist in the absence of lesions on the body and of lesions of lichen planus in this case. As to the question of favus, the lack of actual scarring and the presence of follicular plugs are sufficient to rule out that diagnosis. Moreover, the patient's son, a physician, definitely asserts that there is no history of favus.

#### HERPES ZOSTER GENERALISATUS Presented by DR PAUL GROSS

This man, aged 32, married, born in Estonia, came to the clinic of the Hospital for Joint Diseases on Nov 4, 1935, presenting typical herpes zoster on the left side of the neck. The patient received solution of posterior pituitary on that day and on the following day. On November 6 he was admitted to the hospital because of an eruption covering the entire face and the trunk down to the waist line, marked cervical adenopathy and a temperature of 102.4 F.

The original group of lesions on the left side of the neck had further developed, it had become confluent, and some lesions had become gangrenous. The eruption on the face and trunk was characterized by papules and vesicles with a bright red erythematous halo typical of lesions seen in varicella. The patient was given one injection of a 50 per cent dextrose solution intravenously and three injections of a solution of sodium iodide and was discharged on November 9. The eruption had completely healed, but the patient still complained of pain on the left side of the neck. There were scars at the site of the original zoster, but the lesions which were distributed on other parts of the body healed without scarring.

#### DISCUSSION

DR ARTHUR SAYER Does Dr Gross wish to convey the impression that all of the lesions present are lesions of zoster and are due to the same cause? How soon after the appearance of the typical zoster did the other type of lesions develop?

DR ADOLPH ROSTENBERG Was this patient exposed to varicella?

DR DAVID BLOOM There are a number of reports in the literature about varicella's having developed in persons who came in contact with patients with zoster and vice versa. There are also reports of herpes zoster and varicella occurring in the same person. These facts indicate the probability that zoster and varicella have the same etiologic factor.

DR PAUL GROSS Several years ago I had occasion to observe another case of the same disorder. In that case the herpes zoster appeared in the left frontal region, and after a rise in temperature and marked cervical adenitis symmetrical lesions of zoster type appeared on both ears and on the dorsa of the hands. These cases of herpes zoster generalisatus offer one of the arguments for the identity of the virus of herpes zoster and that of varicella. In answer to Dr Rostenberg, I wish to state that, as far as is known, this patient has not been exposed to varicella.

#### LICHEN PLANUS WITH UNUSUAL FEATURES Presented by DR LOUIS CHARGIN

This man, aged 40, a salesman, states that his eruption first appeared on the forearms about four months ago. It soon spread to the hands, legs and genitals.

There is well marked lichen planus, somewhat subacute in type, affecting the forearms, wrists, palms, lower third of the legs, soles and genitals. On the forearms the lesions are rather large and bluish red. On the palms and soles the

eruption closely resembles keratoderma maculosum palmare et plantare (Buschke and Fischer) The lesions are isolated, scaly at the border and show a well marked central depression Over the heels the eruption is yellowish and hyperkeratotic The nails are markedly affected, being irregular on the surface and showing transverse ridges and flakes There is some subungual hyperkeratosis The mucous membranes of the cheeks are covered with a large number of lesions showing circular arrangement and segments of circles Except for the cutaneous disorder the patient is well He complains of some itching The trunk is free from lesions

## DISCUSSION

DR F E CROSS This is an interesting case, especially because of the lesions on the palms I have seen three or four patients with similar manifestations of lichen planus, but this one exhibits the most characteristic lesions The involvement of the nails is marked Lichen planus of the nails has been recently reported by Dr Frank Vero (ARCH DERMAT & SYPH 26 677 [Oct] 1932)

DR ARTURO L CARRIONN (by invitation) I think it is worth while to state that in Puerto Rico one sees a large number of patients with lichen planus that is atypical in its distribution Often one sees lichen planus of the extensor surfaces, chiefly on the dorsa of the hands In the last two years I have observed three cases of lichen planus of the hands, in one of them there were also lesions on the soles In a particularly interesting case lesions which were not suggestive of lichen planus developed first on both palms, and it was only later, when typical lesions developed farther up on the wrists, that the diagnosis could be definitely established It is not always necessary that the eruption be acute or generalized before one finds lesions on the palms

DR CHARLES A GREENHOUSE What therapy will be instituted in this case?

DR LOUIS CHARGIN In answer to Dr Greenhouse I wish to state that in addition to administration of arsenic it will no doubt be necessary to resort to roentgen therapy, especially for the palmar and plantar lesions If only the lesions on the palms and soles were shown, even the most experienced clinician would most likely miss the diagnosis because the lesions so closely resemble the macular disseminated keratoderma described by Buschke and Fischer

## A CASE FOR DIAGNOSIS (MELANOTIC WHITLOW? SQUAMOUS CELL EPITHELIOMA?)

Presented by DR PAUL GROSS

This woman, aged 59, born in the United States, is presented from the Hospital for Joint Diseases The patient states that two years ago an ironing board fell on her left foot Since then there has been a bluish discoloration under the nail of the left big toe About six months ago the toe increased in size and began to suppurate The distal portion of the left big toe shows a granulating mass with a somewhat verrucous surface surrounded by a hyperkeratotic area The distal portion of the nail is destroyed, the proximal part is raised by the tumor mass and shows a bluish discoloration of the nail bed There is no enlargement of the inguinal glands

Sections from the granulating tumor were taken for histologic study about six weeks ago and revealed a squamous cell epithelioma

The patient is presented because the history and location suggest a melanotic whitlow, while the histologic picture conclusively shows a squamous cell epithelioma The patient is also presented for therapeutic suggestions

## DISCUSSION

DR DAVID BLOOM I agree with the diagnosis of melanotic whitlow on clinical grounds The treatment of choice is, I believe, surgical, and should consist of removal of the toe

DR ARTHUR SAYER In view of the likely serious character of the condition I believe that it is imperative to amputate the toe After that is done, further

pathologic studies should be made to determine the diagnosis more definitely. The loss of the toe should not deter from the indicated therapy.

DR F E CROSS As a prophylactic measure roentgen treatment should be given to the glands in the groin.

DR PAUL GROSS I am thankful for the suggestion. I also believe that amputation of the toe is the method of choice.

NOTE—The toe was amputated on Dec 4, 1935, and the section of the tumor showed melanocarcinoma, the dopa reaction being positive throughout the entire tumor mass.

#### DERMATITIS VEGETANS DUE TO FUNGUS Presented by DR SAMUEL FELDMAN

T F, a youth aged 19, noticed a scaling of the left foot during July 1935. He paid no attention to the condition, and about one month later pruritus of both groins and of the scrotum developed.

On Oct 2, 1935, there were marked redness, scaling and crusting in the interspaces between the third, fourth and fifth toes of the left foot, the involvement extending to the dorsal surface. There was evidence of much scratching and irritation. In both groins and on the sides of the scrotum there were thickening and crusting.

Microscopic examination of scales from the foot revealed short chains of mycelial segments. A culture on a 4 per cent solution of dextrose agar produced a white fuzzy growth similar to that found in cultures of *Epidermophyton*.

The patient received six weekly roentgen irradiations of  $\frac{1}{4}$  skin unit (75 roentgens) each. By the end of that treatment the lesions in the groin became less crusted. After the surface was thoroughly cleansed three oblong patches were seen, each one being made up of a conglomeration of macerated and even ulcerated papules. The condition is somewhat better at present, but it yields to treatment with great difficulty.

The biopsy made on November 17 shows that the epithelial layer is much distorted and thrown into irregular folds. There are intracellular and extracellular edema and marked parakeratosis, and the granular layer is for the most part completely lacking. There are acanthosis and elongation and distortion of the papillae, edema of the corium, vascular dilatation and perivascular round cell infiltration.

## Book Reviews

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**Recent Advances in Dermatology** By W Noel Goldsmith Price, \$5  
Pp 522, with 8 colored plates and 50 illustrations Philadelphia P Blakiston's  
Son & Co, Inc, 1936

This work makes an effort which is new in dermatology, that is to bring together and consider critically the recent essential additions to the knowledge of dermatology in what is the modern period of the various subjects which it takes up and then, as far as may be to interpret in the light of this knowledge various diseases of the skin. For example, it considers the discoveries and advances in the field of allergy which have given the present conception of that reaction and then interprets various diseases in the light of the new knowledge of allergy. The knowledge of the subjects is not merely summarized, as in the usual text-books and year-books, but the discussion covers what may be considered the evolution in the recent period in any field, whether five or twenty-five years.

The first few chapters take up the important new additions to the general knowledge of dermatology, and it is assumed in the discussions which follow that the reader is familiar with these chapters. The author states "Conclusions drawn from evidence sifted in the earlier chapters are taken for granted later. Thus, throughout the rest of the book, a familiarity is assumed with Lewis' work on the Triple Response, dealt with in Chapter I, disorder of Lipoid Metabolism in Chapter VI, cannot be discussed without reference to the Reticulo-endothelial System, which has therefore been made the subject of Chapter V. An understanding of the manifestations of Cutaneous Tuberculosis (Chapter VIII) demands a careful study of the principles of Allergy, which I have tried to disentangle in Chapter VII." The scope of the whole and the method of presentation are indicated by the headings of the chapter, but these hardly indicate the interest of the contents. For example, chapter I is entitled "Blood Vessels," and in this Goldsmith considers extremely interesting new additions to the knowledge in that field. Chapter II is entitled "Glands of the Skin," and Chapter III, "Pigmentation." Both these subjects are commonplace, but with the emphasis on the new knowledge they are made extremely interesting. Other chapters are "Endocrine, Nervous and Mental Influences", "Reticulo-Endothelial System", "Disorders of Metabolism", "Allergy," and "Filter-passing Viruses." There are fourteen chapters in all.

The book is an able and remarkably interesting presentation of the new knowledge of dermatology. It is something unusual in books on dermatology. It integrates the recent advancements in dermatology with the familiar knowledge of this subject, and tends to clarify the knowledge of the principles which underlie pathologic processes and thus broadens one's comprehension of the subject. It can be read universally with profit.

**Year Book of Dermatology and Syphilology, 1935** Edited by Fred Wise and M Sulzberger Price, \$3 Pp 736, with 90 illustrations Chicago Year Book Publishers, Inc

The reviewer is glad to call attention to this volume of the Year Book. These Year Books have for many years been furnishing valuable summaries of the progress of dermatologic knowledge, and this volume maintains the high standard. The editors have selected their material wisely and in all ways have carried out well their responsibilities. One could realize how valuable such a book is in keeping one abreast of dermatologic knowledge only if one tried to review the literature of any topic in dermatology without the aid of such a work. The book deserves circulation among all who have occasion to treat cutaneous diseases.



The editors introduced an innovation last year by beginning the volume with an article of their own on acne. They begin this year's volume with an article on eczema. The innovation seems to the reviewer of questionable desirability. These articles are not properly within the scope of the volume and are apt to be misleading on this point to the reader who takes up the book for the first time. The practice in treating acne and eczema as described in the two articles that appeared in the last two years seems hardly to represent that generally accepted in treating these two troublesome diseases and would be difficult for the practitioner to follow.

**Commoner Diseases of the Skin** By S. William Becker. Price, \$4. Pp. 283, with 83 illustrations. New York: National Medical Book Company, Inc., 1935.

This book covers well the commoner diseases of the skin. The style is didactic (which is a good feature for such a book), and the descriptions are concise and clear. Some chapters are particularly good, for example that on allergy in cutaneous diseases. The book ends with a useful formulary, which is particularly to be recommended because it confines itself to remedies or methods that are in common use and does not confuse the inexperienced practitioner with a multiplicity of little used remedies. The work is of value in furnishing an orientation of the familiar diseases of the skin. The only restriction that must be put on this recommendation is that Becker ascribes to "nervous hyperactivity and exhaustion" in the production of cutaneous diseases an importance far greater than most dermatologists accept. The new student of dermatology will get from his text an exaggerated notion of the importance of the psychogenic and neurogenic factors in diseases of the skin.

**Radium Treatment of Skin Diseases, New Growths, Diseases of the Eyes and Tonsils** By Francis H. Williams. Price, \$2. Pp. 118, with 12 illustrations. Boston: Stratford Company, 1935.

This is a personal book. Coming from Francis H. Williams, it represents the experience of one of the earliest workers in radiotherapy, with both roentgen rays and radium. Dr. Williams wrote a notable book on the subject thirty-five years ago, which was based largely on his own experience, and he has been working in the same field until the present. Unfortunately, only a few pages are devoted to diseases of the skin, but the whole is interesting to any worker in radiotherapy because of the record and wide experience of the author.

### CORRECTION

In the review of "Emotions and Bodily Changes, A Survey of Literature on Psychosomatic Interrelationships, 1910-1933," in the April issue (*ARCH. DERMAT. & SYPH.* **33** 776, 1936), the pronouns "he" and "his" throughout the review should be "she" and "her."

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